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SATURDAY APRIL 16 1955

TABLE OF CONTENTS

Notes on Canadian Medical History H. E. MACDERMOT, M.D., F.R.C.P.(C.) 925
Treatment of Polycythaemia with Radioactive Phosphorus J. B. HARMAN, F.R.C.P., P. L. DE V. HART, M.R.C.P., and E. M. LEDLIE, M.B., D.M.R. 930
Prothrombin and the One-stage Prothrombin Time ARMAND J. QUICK, PH.D., M.D., and CLARA V. HUSSEY, M.S. 934
Cardiac Glycosides in the Treatment of Cardiogenic Shock RICHARD GORLIN, M.D., and EUGENE D. ROBIN, M.D. 937
Lymphangiography J. B. KINMONTH, M.S., F.R.C.S., G. W. TAYLOR, F.R.C.S., and R. KEMP HARPER, M.D., F.R.C.P.Ed., F.F.R. 940
The Dellwood Fire MARIAN E. COX, L.R.C.P.&S.I., D.C.H., BARBARA F. HESLOP, M.D., J. J. KEMPTON, M.D., M.R.C.P., and R. A. RATCLIFF, M.D. 942
The Social and Psychological Backgrounds of Tuberculous Children DINA ROSENBLUTH, B.A., and JOHN BOWLBY, M.A., M.D. 946
Fatal Agranulocytosis During Treatment with Chlorpromazine J. R. TASKER, M.D., M.R.C.P. 950
Cyst Formation Seven Years After a Cutis Graft Repair of Hernia A. G. RUTTER, F.R.C.S.Ed. 951

MEDICAL MEMORANDA

Caeco-colic Intussusception Complicating Perforated Appendicitis. B. A. THOMPSON, M.B., F.R.C.S.Ed. 952
Recovery after Penetrating Wound of the Heart. R. W. LAWRIE, M.R.C.S. 952
Case of Acute Nephritis in Pregnancy. C. MACKIE, M.D., D.Obst.R.C.O.G. 953

BOOK REVIEWS 954

REFRESHER COURSE

Corrosive Poisoning. J. D. P. GRAHAM, M.D., F.R.F.P.S., M.R.C.P.Ed. 962

GENERAL ARTICLES AND NEWS

MODERN ASPECTS OF LIVER AND BILIARY DISEASE 964
REPORTS OF SOCIETIES 968
MEDICO-LEGAL 977
MEDICAL NOTES IN PARLIAMENT 978
VITAL STATISTICS 980
MEDICAL NEWS 981
QUESTIONS AND COMMENTS 983

OBITUARY

A. F. MacCallan, C.B.E., M.D., F.R.C.S. ..975
G. F. Petrie, M.D. 976
O. D. Brownfield, C.B., O.B.E., M.B. 976
E. C. Sprawson, M.C., D.SC., F.D.S. R.C.S., M.R.C.S. 976

LEADING ARTICLES

Canadian Medicine 956
New Patterns of Malaria Control 957

ANNOTATIONS

E.C.T. in Pregnancy 958
Mentally Handicapped Girls 958
Blood Coagulation 959
Psychosomatic Appendicitis? 960
Sicklaemia and Flying 960
Amyloidosis in Rheumatoid Arthritis ..961

CORRESPONDENCE

Primary Aldosteronism. C. L. COPE, D.M., and M. D. MILNE, M.D. 969
Sickling and Malaria. H. M. ARCHIBALD, M.B., and L. J. BRUCE-CHWATT, M.D. ..970

SUPPLEMENT

Full Contents on First Page of Supplement

New Housing Estate Practice in Relation to Established Practices. A. LILKER, M.D. 165
Remuneration of General Practitioners ..166
Correspondence:
Assistants in General Practice. D. E. PEAKE, M.R.C.S.; H. S. SAMUEL, M.R.C.S. 167

CORRESPONDENCE—*cont.*

Carcinoma of Breast. G. C. SAWYER, F.R.C.S.; R. M. BLAIKLEY 970
Low Back Pain. A. STODDARD, M.B. 970
Chicken-pox Quarantine. M. P. K. MENON, M.B. 971
Ovariectomy and Coronary Disease. V. B. GREEN-ARMYTAGE, F.R.C.S. 971
Natural Childbirth. MARY MACK, M.B.; P. M. LEADLEY; ALISON DUDDINGTON; JESSICA DICK READ 971
Carbromal. G. F. NEWBOLD, M.R.C.S. ..972
Chronic Discoid Lupus Erythematosus. J. CHARLES SHEE, M.D. 972
Swallowed Hair-grips. I. ROSE, M.B. ..972
Malignant Melanoma. M. A. W. ROBERTS, F.R.C.S.I., and E. I. KOHORN, M.B. 973
Hypoglycaemia in Chronic Alcoholism. M. M. GLATT, M.D. 973
Tetracycline. A. T. MENNIE, M.B. 973
Epilepsy and the Psychoses. CLIFFORD ALLEN, M.D. 974
Speaking Up. N. A. PUNT, F.R.C.S.Ed. ..974
Night Cramps. H. H. KING, M.B. 974
Hysterical Hyperventilation with Carpo-pedal Spasm. J. CLARKE, M.B. 974
Acute Respiratory Obstruction. K. P. O'SULLIVAN, D.A. 975
Psychotherapy. MURDO MACKENZIE, M.D. 975
Investigations on Everest. L. G. C. E. PUGH, B.M. 975

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY APRIL 16 1955

NOTES ON CANADIAN MEDICAL HISTORY

BY

H. E. MacDERMOT, M.D., F.R.C.P.(C.)

Montreal

A short paper on the history of Canadian Medicine of necessity will be highly selective. I have therefore chosen to deal with a few of its earlier aspects only.

It is natural to date the development of medicine in Canada from the time of the French settlements in the seventeenth century, but the North American Indians had their own medical knowledge, and there is much in it to interest us. Several well-known vegetable drugs, such as sarsaparilla, jalap, cinchona, and guaiacum were native to North America and were used by the aborigines. One writer even gives the Thompson Indians credit for employing organo-therapy in their use of beavers' testicles for pain ; and undoubtedly some tribes realized the value of an infusion of spruce tips in scurvy. Jacques Cartier learnt this from them to good effect. However, their medical knowledge in general is chiefly of ethnological interest.

The Early Practitioners

From the little that is known of the first medical men to arrive in the country, they seem with a few exceptions to have been barber surgeons and apothecaries. They came in the first instance with Champlain on his voyages to Acadia and Quebec, and later with the troops and colonists for New France. By the beginning of 1700 it is said that about 96 people practising medicine were scattered along the shores of the St. Lawrence up to Montreal. Many of these can have been little better than charlatans.

Two names, however, deserve attention. One is Michel Sarrazin (1659–1734), who came out in 1685 as surgeon and later was made chief surgeon to the troops in Quebec. He returned to France to take his degree in medicine, and then returned to settle in Canada, being named royal physician. His practice extended over an area which would have been large even with modern methods of transportation, and there were the added dangers of travelling between Quebec and Montreal. Still, he managed to carry on a great deal of botanical and zoological work, which he réported to l'Académie Royale des Sciences, of which he had been made a corresponding member in the same year (1699) in which Sir Isaac Newton had been admitted. He made a collection of over 200 plants and sent them back to Paris. Tournefort, of the Jardin Royal, forerunner of Linnaeus, named the pitcher plant (*Sarracenia purpurea*) after Sarrazin. He was the first to put the production of maple syrup on a commercial basis and to describe the blueberry. His work on Canadian fauna was extensive and unequalled ; he described the beaver, the porcupine, and the muskrat, which he dissected, but when he came to examine the skunk he failed, because, in his own words, " it had a frightful smell, capable of making a whole canton desert." In his latter days, however, he fell on bad times ; he lost all his money and died a pauper.

Jean François Gaultier (1708–56) was his successor as royal physician, and a worthy one. He too did outstanding work in botany, natural history, and entomology. His name is enshrined in the wintergreen plant, *Gaultheria procumbens.*

Otherwise, men of mark did not begin to appear until the early nineteenth century. They will be mentioned later.

In Ontario, then called Upper Canada, settlements began considerably later. The Treaty of Versailles in 1783 saw the migration of a large number of so-called United Empire Loyalists from across the border. Few medical men came with them to Upper Canada, the explanation apparently being that physicians in the American colonies were not forced out of the country as much as in the case of the other professions. It is probable, too, that the rigours of pioneering life were too severe : as was said, the pioneer physician needed the constitution of a horse and the clothing of an Arctic explorer.

There were not more than 40 qualified men in the province as late as 1815. Quacks flourished. An appeal is found in a Kingston newspaper against quacks " who, without one ray of science, presume to thrust the created into the presence of the Creator."

But gradually better men came in, chiefly retired regimental surgeons, and Boards were set up to control practice, as had been done in Lower Canada (Quebec). Amongst the earliest names of importance are those of James MacAulay ; William Baldwin, who laid out the present Spadina Avenue of Toronto as the approach to his summer home " Spadina " ; the eccentric " Tiger " Dunlop, whose unusual last will and testament is frequently quoted ; and, perhaps most notable of all, Dr. Christopher Widmer. A born leader, Widmer initiated the building of the Toronto General Hospital and was early interested in medical education. He was termed the Father of Surgery in Upper Canada. His name was associated with every medical enterprise, and his energy, ability, and foresight made him a dominating figure till his death in 1858.

Of 260 doctors whose biographies appear in Canniff's *History of the Medical Profession in Upper Canada*

from 1783–1850, 70 were graduates of Scottish universities, 43 of English, 28 of Irish, and 40 of American. Thirty-nine had their training wholly or in part under the system of apprenticeship.

The eastern provinces of Nova Scotia, New Brunswick, and Prince Edward Island were so distinct from Upper and Lower Canada that their early history is quite a separate chapter. They seem to have had no shortage of physicians, as was the case in Ontario. Some were French, but the majority were English, and with the founding of Halifax in 1749 several medical men came into the country. The old churchyards in Halifax have many records of medical interest. One tombstone to two young brothers who died of diphtheria bears the following commentary: "Stranger; whether has the disease or medical omission clad meast in their last claith?"

From 1775 to 1800 there was, as in Upper Canada, a large influx of the United Empire Loyalists, but in this case they were accompanied by many physicians. Nathaniel Perkins, one of the first to practise variolation in Boston; W. J. Almon; and the Hon. John Halliburton were all prominent men. The name of Abraham Gesner is outstanding. A native of Nova Scotia, he had studied under Abernethy and Astley Cooper. His work in geology and natural history was notable. He discovered coal oil, inventing the word "kerosene" for it. His old refinery still exists, and is owned by the Standard Oil Company.

In the West there were pioneer doctors with the fur-trading establishments as early as 1814. Dr. (Sir) John Schultz built the first house in Winnipeg. He later became the Lieutenant-Governor of Manitoba, and in welcoming the Canadian Medical Association at one of its early meetings in the West (Banff) exhorted them to "pause and reflect for a moment that they were where for economic purposes Canada was widest, and no longer a mere arable strip on the banks of the St. Lawrence."

In the North-West Territories, which comprised what is now Alberta and Saskatchewan, there were occasional medical men with explorers and fur-trading settlements. Dr. J. Richardson, with Sir John Franklin in his overland journey to the Polar sea, makes a reference to Edmonton in 1820 (it had been founded in 1795 as a fur-trading centre) as having much goitre, and Dr. W. B. Cheadle treated patients there on his transcontinental journey.

With the formation of the Northwest Mounted Police (the "Mounties") in 1873 a regular succession of surgeons began, the first being Dr. George Kittson. Dr. R. G. Brett (1851–1929), Ontario born, helped to found the Manitoba Medical College, then moved to Alberta and became a leading medico-political figure. He established the sanatorium at Banff.

The building of the Canadian Pacific Railway (finished in 1885) brought yet more medical men into the country, and by 1889, the year in which the Canadian Medical Association held its meeting in Banff, there were 33 physicians registered in the N.W.T.

There is no difficulty in naming the pioneer doctor in British Columbia. This was Dr. John S. Helmcken (1825–1920), a graduate of London, who came to British Columbia in 1850, as surgeon to the Hudson's Bay Company. At one period he described himself as "the leading practitioner from San Francisco to the North Pole, and from Asia to the Red River of the north." This was easily accounted for, as he was then the only practitioner within those limits. He filled a large place in the medical and political life of British Columbia, and his house in Victoria is preserved as a museum. He was one of the delegates to Ottawa from the province to support terms of union with Canada.

Medical Teaching

As the better type of men increased medical boards were set up for the control of medical practice (in Lower Canada in 1788; Upper Canada in 1795; Nova Scotia in 1828), but these had little control over the large numbers of unlicensed practitioners. Often these latter were the only form of practitioner available under pioneering conditions. There was no medical teaching in the country, as would be expected. The Canadian medical student had either to be satisfied with the training of an apprentice or else go abroad at great expense.

At this very early stage of development a well-organized medical school was formed in Montreal in association with a general hospital to provide clinical teaching. The teachers—four Edinburgh graduates—were the staff of the Montreal General Hospital, founded in 1819, and their school, which was opened in 1823, was at first called the Montreal Medical Institution. In 1829, however, the school agreed to become the Medical Faculty of McGill University, thereby gaining the right to confer degrees, whilst enabling the University to begin active operation as required by the terms of its foundation.

This school owed its formation to the desire of its four founders to raise the professional standards in Canada. The names of the four founders were John Stephenson, A. F. Holmes, William Robertson, and William Caldwell. They were men of strong personalities. Caldwell had fought a duel over some derogatory comments on the first proposal to build the hospital. Holmes became the first dean of McGill Medical Faculty, but was no more influential than the more reserved Robertson. Stephenson apparently was the *vis a tergo* in the organization of the school. As a student he had the distinction of being the first to be operated on by Roux, of Paris, for cleft-palate, and his Edinburgh graduation thesis *De velosynthesi* is still preserved in the Osler Library at McGill.

These men left their mark on the school by their transmission of the Edinburgh tradition of clinical teaching in the wards. This school has the longest uninterrupted record of bedside teaching in North America*; it was what attracted Osler to McGill.

The first attempt to form a medical school in Ontario was made by Dr. John Rolph in 1824. Rolph was at once a politician, which got him into a great deal of trouble; a member of the Bar, which probably helped him out of trouble to some extent; and a well-trained surgeon. He had studied under Astley Cooper and had great attainments as a lecturer. He became involved in the rebellion of 1837, fled to the States with a price on his head, and was finally pardoned in 1843, when he came back to Toronto and began his school again. He gathered good men around him, notably Dr. Joseph Workman (1805–94), who probably had more brilliant mental powers than Rolph himself. Rolph's school was eventually taken into the University of Toronto in 1887. There were two other private medical schools in Toronto for a time which also merged with the University.

Even when they became medical faculties of universities the older medical institutions remained largely independent for many years, making their own appointments and controlling their own finances. The right to grant medical

*Clinical teaching at the bedside had been carried on at the Pennsylvania Hospital in 1756, but it was interrupted by the War of Independence and was not resumed in the Edinburgh tradition until Osler went to Philadelphia in 1884. Macphail rightly speaks of "two faint streams from Edinburgh across the Atlantic, one to Philadelphia and one to Montreal" ("Sources of Modern Medicine," *Canad. med. Ass. J.*, 1933, **28**, 239).

degrees, however, was always retained by the universities. This discouraged the formation of weak and undesirable institutions.

The following is a list of the Canadian Medical Schools in geographical order from east to west :

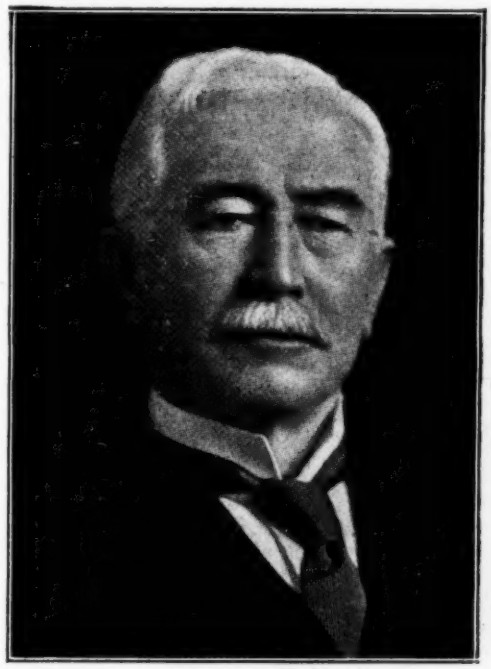
Established Canadian Medical Schools

	Founded as a Medical Faculty or School in
Dalhousie University, Halifax, N.S.	1868
Université Laval, Quebec City	1853
Université de Montréal, Montreal, Que. ..	1843
McGill University, Montreal, Que.	1823
University of Ottawa, Ottawa, Ont.	1945
Queen's University, Kingston, Ont.	1854
University of Toronto, Toronto, Ont.	1844
University of Western Ontario, London, Ont.	1881
University of Manitoba, Winnipeg, Man. ..	1883
University of Saskatchewan, Saskatoon, Sask.	1926
University of Alberta, Edmonton, Alta. ..	1913
University of British Columbia, Vancouver, B.C.	1950

Up to 1914 those seeking postgraduate training still turned almost wholly to British and Continental centres, French-speaking doctors in particular going to Paris. The first world war checked this severely. The second war ended it altogether as regards the Continent. The great expansion in hospitals and research centres in the U.S., but also in Canada in such institutions as the Montreal Neurological Institute and the Banting and Best Institute in Toronto, has reversed the direction of postgraduate migration.

No university degree in medicine of itself confers the right to practise in Canada. Each province retains the control of licensure within its boundaries. Some schools require their students to register with their home province before beginning their course. Even this registration, however, only gives the right to practise in that particular province.

There were many years of discussion before the provinces agreed on a uniform registration which would permit of Dominion-wide practice. This was one of the first objectives of the Canadian Medical Association when it was formed in 1867, but it was only achieved in 1912 by the persistence and statesmanship of Dr. (Sir) Thomas Roddick (1846–1923) after his election to the Federal legislature.



Sir Thomas Roddick.

A Newfoundlander by birth, Roddick had early shown his outstanding capacities. It was he who first brought Lister's methods convincingly before the profession in 1877.* In 1885 he was put in charge of the medical services in the Riel Rebellion in Saskatchewan, work which required not only organizing ability but unusual physical endurance, for which his powerful physique was well prepared. His real genius, however, lay in the patience and imperturbability by which he was able finally to harmonize apparently irreconcilable views and to persuade men to rise above provincialism. Roddick evolved the Canada Medical Act (the "Roddick Bill"), by which a medical register under a Dominion Medical Council was set up. Those passing an examination set by the Council were to obtain the right to register for practice in any province without further examination, on complying with the regulations pertaining thereto. Thus the right of the provinces to control their licensure was not disturbed, whilst it did away with the necessity for taking separate examinations for each province to which a man might wish to go.

In the carrying out of this Dominion registration certain complicating factors have arisen in late years, chiefly relating to the large numbers of medical men from other countries seeking to practise in Canada. But there has been no change in the general tenor of the legislation.

*Sir Thomas was the first medical man outside of the British Isles to be chosen as President of the B.M.A. This was on the occasion of the first visit of the B.M.A. to Canada in 1897.

Newfoundland

The union of Newfoundland with Canada (1949) is too recent for the inclusion of its medical history in this sketch. It may be said, however, that the first colonists to reach Newfoundland (1610) had no medical men with them. The comment by Guy, the leader of the expedition, after ten months in Newfoundland, was that only four had died during the winter, and in his opinion "all of them if they had as good will to work as they had good stomachs to their victuals would long since have been recovered."

The first medical men came with a French military force in 1662, and military surgeons came and went with the various expeditions. Dr. William Carson, an Edinburgh graduate, has left a name for his fearlessness in urging reform in the government of the island, and was chiefly instrumental in having the first hospital for civilians built in St. John's in 1813. Before that, two military hospitals existed (one for infectious disease), but they were almost exclusively for the soldiers of the garrison.

Hospitals

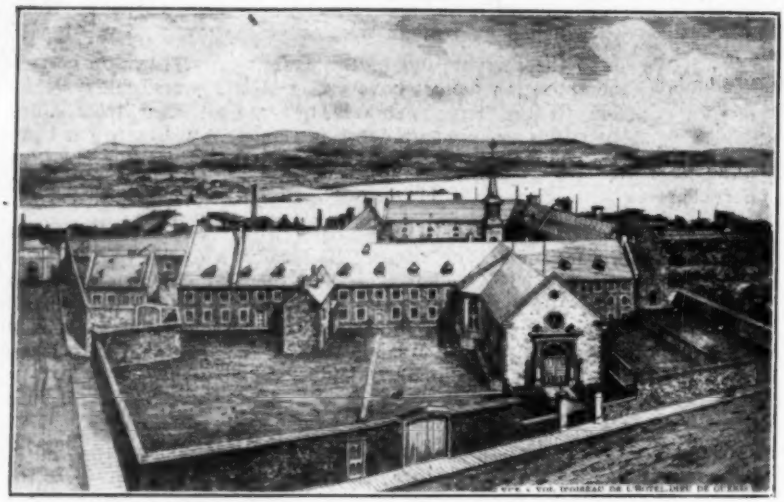
The first hospitals in Canada were built in the stormy years of the French settlements in the seventeenth century at Quebec and Montreal, and later at Three Rivers. The oldest is the Hôtel-Dieu of Quebec, begun about 1641, but suffering many vicissitudes from attacks by the Indians.

The Hôtel-Dieu of Montreal was built first in 1644, and was due entirely to the courage and ability of Mlle. Jeanne Mance. She had no training as a nurse, but devoted herself to the care of the sick of the small colony. The hospital suffered much from poverty. It was burnt down three times. In 1861 it was moved uptown from its site in the business section, and has become greatly enlarged and completely modernized.

The oldest English hospital in Canada is the Montreal General Hospital. It was founded in 1819 and its original building was erected in 1822. It arose as a direct result of the rapid growth of Montreal, and of the floods of immigrants arriving in Canada in the post-Napoleonic period. It was a teaching hospital from the beginning, as already mentioned, and for about 60 years was the only English hospital in the city. Osler studied in its wards and later was one of its physicians. Much of the material for his original *Textbook of Medicine* was drawn from his experience in its wards and necropsy room. The hospital is now being transferred to a more suitable site uptown.

The Royal Victoria Hospital, the second teaching hospital to appear in Montreal, was opened in 1892, and immediately began to build up a first-class staff. In the last 50 years there has been a tremendous expansion in hospitals in the city and province.

In Toronto (first called York) the Toronto General Hospital was built in 1820, but was taken over by the Provincial Government for parliament buildings in 1824,



L'Hôtel-Dieu de Québec in 1816. The walls date from 1696.

and was not used as a hospital until 1829. The T.G.H. has seen many changes and difficulties before becoming the present very large and modern institution (1,418 beds).

Toronto can claim the honour of having established the first hospital for children in the Sick Children's Hospital. Beginning in small rented quarters in 1875, it has gradually been built up into an institution of international reputation.

It was in the Department of Physiology of the University of Toronto that Banting and Best did their original work on insulin in 1921. The Banting and Best Department of Medical Research was established by the Board of Governors of the University as the result of a special grant made by the province of Ontario in 1923.

Medical Journals in Canada

The first Canadian medical journal, *Le Journal de Médecine de Québec*, was published in Quebec in 1826 by a young French doctor, F. X. Tessier. It had both French and English papers, and was well conceived; but it was much too far ahead of the medical strength of the country, and ceased in 1828.

It was 1844 before the appearance of the next journal, the *Montreal Medical Gazette*. Although it lasted for only a little more than a year, it was the beginning of a series of publications which managed to maintain medical journalism in various guises until some degree of permanence was attained. It was as difficult then as it always has been to find men both capable of editing and willing to make the necessary sacrifices. Two men stand out in the early years.

Dr. Archibald Hall, of Montreal, started the *British-American Journal of Medical and Physical Science* in 1845, and for eight years waged a losing battle against a small circulation and lack of funds. But he produced a first-class journal, which reflects his championship of high standards, his courage and dignity, and his absolute certainty that he was always in the right. He strongly reproved the profession for failing to support him even after a second venture later on; but he seems to have been too dictatorial, too bitter, and too easily irritated to carry on a journal successfully.

In contrast there was Dr. John Fulton, of Toronto, who edited *Canada Lancet* (1868–1922)—first called the *Dominion Medical Journal* (1868–9)—from 1872 to 1887, and drew high praise from Osler for his publication. It was successful because he was methodical and business-like, even if it lacked the fire which warmed the pages of Hall's journal. As Osler said, Fulton learned the lesson "that success cometh neither from the east nor from the west, nor yet from the south, but is found in close attention to the everyday details of life, no matter how trivial."

Several French journals have been produced. *L'Union Médicale*, begun in 1872, has the record for the longest uninterrupted publication under one title. But the *Canadian Medical Association Journal* has an older lineage. Its progenitor was the *Canada Medical Journal and Monthly Record of Medical and Surgical Science*, which first appeared in 1864. The two editors, George Fenwick and G. W. Campbell, parted company in 1872, owing to "personal differences," and each then carried on a journal of his own under slightly different names. Campbell's journal, the *Canada Medical Record*, was very much his own affair, and ceased with his death in 1904. But Fenwick learned the wisdom of teamwork and was able to attract to the staff of the *Canada Medical and Surgical Journal* the best men in the Montreal profession. Under the later title of the *Montreal Medical Journal* it reached great heights in the journalistic field, especially under the editorship of Andrew Macphail, who exploited to the full his clear and pungent style. In 1910 the proprietors of the journal agreed, in the interests of organized medicine, that it should become the *Canadian Medical Association Journal*, along with the *Maritime Medical News*, a Halifax publication. The difficulties which beset the journal in the war years are mentioned later; it need only be added that its editorship was undertaken in 1921 by Dr. A. D. Blackader (1843–1932), as Macphail had resigned on account of ill-health. Dr. Blackader, who was then in his seventies, gave himself whole-heartedly to the work of building up the journal, and when he resigned in 1930 he had placed it on a solid foundation.

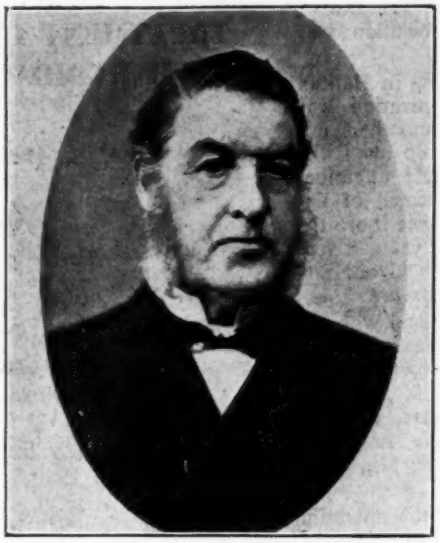
A total of 72 periodicals have appeared in Canada in the course of 128 years. At present there are 18, including provincial Bulletins and undergraduate publications. Medical journals are not now undertaken with the apparent light-heartedness of last century. The economic implications are too severe, and advertising support is indispensable in almost every instance.

The Canadian Medical Association

The desire to organize the profession in Canada arose several years before the time was ripe for carrying it out. In 1844 Dr. Joseph Painchaud, of Quebec, suggested the

The Montreal General Hospital as it was when Osler was a student there.

formation of a "Medical Fund or Association" whose main object was to be a charitable one. The *Montreal Medical Gazette* (the earliest Montreal medical journal) at once proposed to widen the scope of the Association to include the dissemination of medical information and to obtain representation of its wants in legislation. The two medical societies of Toronto and Montreal then combined in developing the movement, with Dr. F. Badgley, of Montreal, as one of the most active leaders.



Sir Charles Tupper in 1891.

Dr. Palmer Howard, outstanding in the early days of the C.M.A.

However, friction developed between the medical societies and the so-called "districts," and the movement failed utterly. Another attempt four years later began in a better spirit, but lacked organization enough to get beyond the first meeting. The wonder is that these efforts were made at all. Communications were difficult, and the number who realized the value of organization was very small. The eastern provinces were not approached in the matter at all.

The third attempt followed on, though it was not directly the result of, the political union of the Canadian provinces in 1867. Dr. William Marsden, of the Quebec Medical Society, who had taken part in the earlier abortive attempts, was now the first to realize, or at any rate to act on, the more favourable prospects for medical organization which would arise from confederation. He was further stimulated by a visit he had paid that year to a meeting of the American Medical Association, as delegate from the College of Physicians and Surgeons of Quebec, bringing back reports of what was being proposed in regard to education and licensure.

His report was taken up by the Quebec Medical Society, and a committee, composed of Drs. J. A. Sewell, William Marsden, R. H. Russell, P. D. Tessier, L. J. A. Simard, F. H. A. Larue, and H. Blanchet, drew up an appeal to all members of the profession in Canada (now nearly 3,000) to meet in Quebec for the organization of an Association. The chief object named was that of medical legislation.

This time there was no hesitation. On October 9, 1867, 167 medical men met in Quebec, including representatives from Upper and Lower Canada, as well as from Nova Scotia and New Brunswick, and the organization of the Association was successfully completed, with Dr. (Sir) Charles Tupper as president.

The first annual meeting was held in Montreal, again under the presidency of Dr. Tupper, of whom Osler has said that he was a brilliant example of success of the doctor in politics, although "he never really served two masters—he was a politician first and a practitioner only when stranded by the exigencies of party." The value of his experience to the Association in its formative years was inestimable. His physical attributes were remarkable. He lived to the age of 94 and actually "stumped the country" for his party in his 80th year, and successfully, too. And yet he had been ready at the age of 59 to give up all activities, as he was believed then to have Bright's disease. His case was mentioned by Osler in his paper "On the Advantages of a Trace of Albumen and a Few Tube Casts in the Urine of Men above 50 Years of Age" (*N.Y. Med. J.*, 1901, **74**, 949).

It should be added that Dr. Marsden, who was rightly called the Father of the Association, refused nomination even as vice-president. Extremely retiring in disposition, he preferred to work without recognition, but did accept the presidency in 1873.

The Association immediately began to discuss the problem of medical education and licensure. The first proposal favoured an Act similar to the Medical Act of Great Britain, setting up a general council of medical education for registration. No other subject occupied more of the time of the Association in its early years, and none gave rise to more frustration. In 1874 it was dropped altogether, by common consent, fully vindicating the reflection of Dr. Joseph Workman, of Toronto, that "our greatest, and alas, too palpable want is Union—honest, earnest, self-sacrificing Union—and our next great want is prudence."

The other subjects dealt with at the first meeting were those of statistics and hygiene, and the formulation of a code of ethics. It was only in the third year that a programme of scientific papers was presented. In the tenth year the scientific proceedings were published in printed form; the secretary of the publications committee that year was William Osler.

The Association took some credit to itself for its continuous representations to the Government on the necessity for centralizing the control of public health. Its records show an appreciation of the Government's action in finally establishing a Department of Public Health in 1919.

It is of interest that a proposal was made in 1876 in favour of uniting the Canadian and American Medical Associations. After due consideration, however, and the expression of most cordial feelings on both sides, it was decided to let the matter drop, and merely to continue to exchange courtesies by sending delegates to each other's meetings.

The Association has had its difficult periods. At the end of the first 25 years, for example, interest in it seems to have sunk very low, even to the point of a suggestion in 1893 that it should disband. Membership was small, and only a faithful few carried on the work, notably men like LeBaron Botsford, of St. John, N.B., E. M. Hodder, W. H. Hingston, H. S. Birkett, Joseph Workman, R. P. Howard, F. N. G. Starr, and Alex McPhedran.

Then it gained new life, and in 1910 an Association journal was begun with Dr. (Sir) Andrew Macphail as editor. But just as the journal was getting well under way the war broke out. The editorial staff went overseas on active service, along with a good many contributors, and only the devotion of one or two unofficial editors, notably Dr. Maude Abbott, kept the journal going, whilst the Association itself had great difficulty in carrying on. No

meetings were held in 1915 and 1916, and by the end of the war the financial position of the Association was extremely bad.

The turning-point came at the annual meeting in Halifax in 1921. It was realized then that reorganization was essential. The various provincial organizations had not been brought closely enough into relationship with the Association, and the finances needed immediate attention. A full-time secretary was appointed in the person of Dr. T. C. Routley, a bond issue was raised, and once more the Association began to expand. Within a few years it had paid off the bond issue and was showing the vigour and growth which has brought it to its present stature.

The Association has continued not only to deal with the profession's educational and economic problems, but to concern itself with social and political developments. Post-graduate lectures were first organized in 1925, and were carried on throughout Canada for seven years, with the help of generous grants from the Sun Life Assurance Company. A Department of Hospital Service, also aided by this company, was carried on for 20 years.

Health insurance has probably occupied the attention of the Association more continuously than has any other subject. The principle of insurance against the cost of illness has received the support of the Association, particularly through the medium of prepaid medical care plans.

The first proposals to establish a Royal College of Physicians and Surgeons of Canada were made at the annual meeting in Vancouver in 1920, the primary object being to stimulate study and postgraduate work in medicine and surgery. The idea gradually matured, and the College was finally incorporated by Act of Parliament in 1929. Once launched, the College became an entirely independent organization.

Inspection and accreditation of hospitals is one of the later activities of the Association. This work had previously been done in Canada by the American College of Surgeons, and on their withdrawal from this particular field the Association initiated plans for the necessary machinery to carry it on. To Dr. E. K. Lyon, of Leamington, Ont., is due most of the credit for focusing attention on the importance of this phase of hospital life and of eventually bringing into being the Commission to deal with it. The C.M.A. contributes the major part of the very heavy cost of this work. Formation of a College of General Practice originated within the Association some five years ago, and the College came into being last year, with a full-time secretary. There has been an encouraging response to this movement, but of course it is still at a very early stage of development.

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There is little information on the growth and physical development of Indian children, according to the latest annual report of the Nutrition Research Laboratories at Coonoor. However, a start has been made. Workers at the Coonoor Laboratories first analysed data in the literature on 46,000 boys from various parts of India, and from this prepared growth curves for them. Then a homogeneous group of about 2,000 boys were examined from around Coonoor, and their growth curve was found to correspond closely to that derived for India as a whole. But, what is more interesting, these curves were found to parallel, though at a slightly lower level, recent growth curves for British and American boys. The report poses the question of the influence of nutrition in producing the lower growth progression found in the Indian children.

TREATMENT OF POLYCYTHAEMIA WITH RADIOACTIVE PHOSPHORUS

BY

J. B. HARMAN, F.R.C.P.
Physician

P. L. de V. HART, M.R.C.P.
Formerly Senior Registrar

AND

E. M. LEDLIE, M.B., B.S., D.M.R.
Clinical Research Radiotherapist
The Royal Marsden Hospital

Polycythaemia was first treated by radioactive phosphorus (P^{32}) in 1940 by Lawrence, who has reported 201 cases dealt with since that time (Lawrence *et al.*, 1953). Two reports have already been made in this country, comprising 20 cases (Bodley Scott, 1953) and 27 cases (Abbatt *et al.*, 1954). P^{32} was used in the Royal Marsden Hospital at the end of 1948, and 48 cases have been treated since then. Our purpose is to draw attention to the benefits that may be expected and to comment on certain features of the symptomatology and course.

Radioactive phosphorus is prepared by the irradiation of pure sulphur, and is obtained as a solution of orthophosphoric acid. It has a half-life of 14.3 days, but excretion of part of the administered dose in the urine reduces its effective half-life in the body to about 10 days.

When P^{32} is administered the phosphorus participates in the general biochemical reactions of the body. A large amount is incorporated into those cells in which proliferation is most active, because this is where the *turnover* of phosphorus is greatest. One of the most active tissues in this respect is the bone marrow, and this activity is increased when there is marrow hyperplasia as in polycythaemia or leukaemia. The injection of radioactive phosphorus therefore provides a method of irradiating the overactive haemopoietic tissues more selectively than can be done with external irradiation.

Dosage

The patient is admitted to hospital. The P^{32} is injected intravenously as a solution of sodium phosphate. There are no side-effects and no irradiation reactions have been observed, even following the administration of the maximum dose. After the P^{32} has been given, the urine is collected and its radioactivity measured. The patient is discharged from hospital when the excretion has reached a safe level (100 mC in 24 hours), which in practice means two to three days after the injection.

Two methods of P^{32} dosage have been employed. At first all patients were treated by a "split" dose—that is, two injections of P^{32} at an interval of about two months. Subsequently it was thought that a single injection would probably be sufficient for some patients, and both methods are now used according to the severity of the disease. The split dosage was used for 28 patients, with an interval of 6–12 weeks between the injections. The dose was usually 5 mC followed by 4 mC. The smallest amount given in the two injections was 6 mC and the largest 12 mC. A single injection was given to 16 patients as the first treatment. The dose varied between 4 and 7 mC, according to the severity of the symptoms and haematological findings. The single dose is more convenient, and, since there is no obvious difference

in the results, it is used whenever possible, and almost always in the treatment of relapse. Further treatments are usually required every one or two years throughout the duration of the polycythaemia. The largest total amount of P^{32} given to one patient to date is 36 mC.

The inhibition of the bone marrow persists in most cases for a year or more. But the effect on the circulating red-cell mass, and hence on the symptoms, becomes apparent only gradually, in the course of two to three months. If this period of gradual improvement is added to the period of gradual worsening before treatment is again worth while, it may be found that a patient who needs treatment once a year is properly controlled for only two-thirds of the time. In order to shorten the period of improvement we have done a massive venesection at the same time as injecting P^{32} on 48 occasions when the patient has had a notably high red-cell mass. This is made possible only by a simultaneous infusion of a plasma substitute to prevent shock and heparinization to keep the blood flowing. By this means it is possible to bring the haemoglobin down to a normal figure in one operation. The most that has been removed is 5 litres, replaced by 3.6 litres of dextran: the haemoglobin fell from 155% to 94%. It has been found best to reduce the haemoglobin to slightly below normal, since the excretion of plasma substitute in the next 48 hours usually causes it to rise again by about 10%. The replacement should be a half to one litre less than the quantity withdrawn; a rise of pulse rate shows that insufficient plasma substitute is being replaced. It is advisable to keep the patient in bed for a day and forbid solid food, lest fainting or nausea occur.

Present Series

The distribution by age and sex is shown in Table I. It is very difficult to determine the age at which polycythaemia develops, since for a time there may be no symptoms, and

TABLE I.—*Age When First Seen at the Royal Marsden Hospital*

Age:	30–39	40–49	50–59	60–69	70–79	80+	Total
Male ..	3	5	8	5	2	1	24
Female	1	4	3	10	5	1	24
Total	4	9	11	15	7	2	48

even when they occur they are often too mild to send the patient to a doctor. For example, a woman first diagnosed at the age of 39 said she had had symptoms since adolescence, and it was clear that her symptoms were due to polycythaemia. Perusal of the histories suggests that the disease was present for an average of four to five years before it was diagnosed.

The frequency of the various symptoms is shown in Table II.

TABLE II.—*Main Symptoms of Above 48 Cases*

	Cases	%
High colour	48	100
Haemorrhagic phenomena	27	56
Dyspepsia: all cases	17	35
" cases with D.U. on *x*-ray film	6	12
Splenic pain	14	29
Pruritus	17	35
Thrombosis: venous	8	17
" arterial	9	19
Dyspnoea, headache, dizziness, etc.	10	21
Ulceration, chronic sepsis, or gangrene	9	19

The high colour is most evident on the face, but is here an unreliable diagnostic guide. It is best to examine the conjunctivae, tongue, nail-beds, and especially the palms of the hands, in which high colour is at least as reliable a guide as an isolated blood count. A complaint of red eyes was not uncommon, and a few patients had been treated for "conjunctivitis" over many months: but soreness was present in only one case. Telangiectases were common on the cheeks. The heightened colour has a distinct purplish tinge, which is, in fact, the natural colour of concentrated oxyhaemoglobin and is not necessarily due to the presence of reduced haemoglobin.

Thromboses and haemorrhages were both common. Arterial thromboses were found in those sites where their occurrence is most easily detected—that is, in the retina, internal capsule, pons, and the coronary, femoral, and popliteal arteries. Venous thromboses were common in the legs. Haemorrhages occur from the nose, upper and lower gastro-intestinal tract, ruptured varicose veins, gums, and as ecchymoses. Prolonged bleeding is also apt to occur after dental extractions and operations. Both thromboses and haemorrhages might occur at the same time, with a normal or high platelet count and no demonstrable abnormality of coagulation or prothrombin generation. It is probable that the haemorrhages are due to some capillary abnormality.

Dyspepsia had the usual characteristics of peptic ulcer, and a duodenal ulcer was demonstrated in 6 of the 17 dyspeptics. Pruritus was usually generalized and always worse in the palms and soles; it is aggravated by a hot bath. Chilblains, ulceration, sepsis, and partial gangrene of the toes were common and occurred in cases with apparently normal vessels. Other symptoms commonly complained of were dyspnoea, faintness, palpitations, headache, thumping in the head, dizziness, fatigue, lethargy, and a congested feeling in the face and head. Splenic pain was due either to infarction or to the weight of the tumour. The spleen was definitely enlarged in 27 of our cases and was below the umbilicus in 9.

Haematology

The most reliable measures of red-cell concentration both at the Royal Marsden Hospital and elsewhere have been the haemoglobin or packed cell volume. The red blood cell count has commonly been extremely variable and unreliable, which is probably due to the difficulty of homogenizing samples properly. No patients were regarded as polycythaemic unless the readings were well above normal—for example, Hb, 130%; P.C.V., 60%; R.B.C., 7,000,000. As is well known, there is usually an increase of polymorphs, with a few metamyelocytes, and less often of platelets. These associated changes are best seen in marrow puncture or biopsy.

Blood Volume

The ordinary methods of haematology measure the concentration of red cells or haemoglobin, and in polycythaemia the concentration is of course raised. The essential pathological change, however, is an increase in the red cell mass, and this can be deduced from measures of concentration only if it is known that the plasma volume remains constant. It would therefore be desirable to have simple and accurate methods of measuring both the red-cell mass and the plasma volume that could be used in clinical medicine. Unfortunately, the measurement of blood volume is attended by considerable theoretical and practical difficulties. Until recently the usual method was to measure the plasma volume by dye dilution and to deduce the red-cell mass from the haematocrit. Radioactive tagged protein fractions of normal plasma can now be used. The plasma volume, however, is not a constant quantity, because water passes in and out of the capillaries in various states of body activity. The same applies to some extent to any substance used as a marker. Moreover, the venous haematocrit is not an accurate measure of the proportion of cells to fluid in the vascular system as a whole. The ratio of cells to fluid is different in arteries, capillaries, and veins, where the rate of flow is different, and the distribution in these compartments will also vary with differing states of body activity. It is, however, now possible to measure the red-cell mass directly by tagging cells with radioactive iron, phosphorus, or chromium. These measurements are simple and fairly accurate, and so the plasma volume is best deduced from the red-cell mass and haematocrit, using appropriate correction factors.

These observations may be sufficient to show why there is no wide and accurate knowledge of blood-volume changes in polycythaemia. It is generally thought that the plasma

volume tends to be unchanged or even to be diminished as the red-cell mass increases until high haematocrit levels (55% ±) are reached (Mollison, 1951). Our limited observations show that this is usually true, though patients with high haematocrit levels (over 75%) may also have a low or normal plasma volume. Measures of the red-red concentration, by haematocrit or haemoglobin estimations, are therefore usually proportional to the red-cell mass, but this is not always the case. One of our patients has a greatly increased plasma volume, so that he is plethoric though not polycythaemic as ordinarily defined.

We have found that the chromium method is simple to use and consistent in its results, and we are now defining normality in this way. Patients with normal concentration may still retain a plethoric appearance of the face, eyes, and especially of the palms. This does not indicate a raised total blood volume, but is due to an irreversible dilatation of the skin venules.

Diagnosis

The long time that elapsed before some of our cases were diagnosed suggests that polycythaemia is not always readily detected—which is probably due to its rarity or to unfamiliarity with the symptoms.

Once polycythaemia has been recognized there appears to be little difficulty in distinguishing cases that are secondary to heart or lung disease. Doubts may exist where there is emphysema and no splenomegaly, but they are usually settled by the state of the bone marrow. A mistake was made in a man who had gout, nephritis, and multiple arterial abnormalities. Despite his normal marrow he was eventually treated with P^{32} 3 mC and venesection, which threw him into right heart failure. Cardiac catheterization showed that he had a persistent ductus with flow reversed owing to pulmonary hypertension.

Cases are not accepted for treatment unless they are actually polycythaemic when seen. In some cases the only evidence presented has been a raised red-cell count, which is fallacious. It is also just possible that long remissions may occur naturally or with conventional treatment—one man, a roving Irish labourer, had been treated for 13 years at six different hospitals with venesections and phenylhydrazine, but was quite normal for the year and a half that we observed him. Two other patients who undoubtedly had a marrow dysplasia were diagnosed for many years as cases of polycythaemia, which they may well have had; but they had none with us, and one became leukaemic and the other is probably developing myelofibrosis.

Course and Prognosis

The natural history of polycythaemia is probably not completely known. The disease is not common, its course is very long, and the sufferers have not previously been collected into special clinics. It is usually regarded as a disease of older persons that remains with them till they die or are killed by a stroke, which is the natural termination of the disease. This is true of most cases, but exceptions are common enough to deserve mention. The early age at which it may occur has been noted. The other exceptions are those that develop leukaemia or myelofibrosis.

Transition into myeloid leukaemia is not uncommon; the change from leukaemia to polycythaemia is rare but has occurred in our series. Others become anaemic owing to replacement of the bone marrow with reticulum cells or fibroblasts. Anaemia may also be due to haemolysis, which can be stopped by splenectomy as in leukaemia and lymphadenoma. In some cases the erythropoietic tissue is not confined to the bone marrow, but is found in the liver and spleen, and may even form sizable discrete tumours elsewhere which erode bone. The production of polymorphs and platelets is usually both increased and abnormal, and in some the platelet level is so high that the diagnosis of essential thrombocythaemia might have been made with equal justification.

Observations of this sort have made it impossible to maintain concepts of polycythaemia, leukaemia, myelofibrosis, and so on as separate diseases, though the terms are retained for convenience. The present tendency is to regard them as possible manifestations or phases of a neoplastic disease that affects primitive mesenchyme cells. Although polycythaemia may be but a phase, it is clearly one that is both stable and benign, so that once patients enter into it they are likely to remain in it for the rest of their lives.

These considerations have some bearing on treatment, especially with radiation. Radiation can play a part in the causation of both leukaemia and marrow aplasia. Can it be held responsible for the leukaemia and myelosclerotic terminations of polycythaemia? Leukaemia is known to supervene without radiation therapy, and it has been estimated that its frequency is no greater after P^{32} (Lawrence *et al.*, 1953; Stroebel, 1954). One of our cases became leukaemic, and another is probably going that way. The evidence for myelosclerosis is less certain because of its rarity. But cases certainly occurred before the advent of P^{32}, and the replacement of erythroid tissue by reticulum and fibrous tissue, such as occurs with myelosclerosis, has not been seen after radiation aplasia. One of our cases developed myelosclerosis and another probably did.

Another point is that though P^{32} is indicated in the polycythaemic phase it may be harmful in another. Leukaemia usually develops quite suddenly, and there is no difficulty in detecting its onset. In contrast, the patients who are developing myelosclerosis appear at first to be in a satisfactory remission lasting a year or so. Eventually the blood count sinks below normal and they die despite transfusions. We have been somewhat uneasy about five of our patients whose remissions have lasted more than two years. But two with the longest remissions, over three and over four years each, have now become polycythaemic again. It appears that a fall below the normal haemoglobin is the ominous feature, not the length of remission.

Effect of Treatment

The objects of treatment are to prevent disastrous vascular accidents in the central nervous system and to relieve the patient of annoying symptoms.

Our own observations are not sufficient to prove that major thromboses have been prevented, though none has occurred since treatment. Stroebel (1954) has shown from a ten-year study of 241 cases that the expectation of life is increased with treatment. Most symptoms are completely relieved when the blood count is controlled. This applies particularly to ulceration and sepsis of the toes, haemorrhagic phenomena, the various "congested" feelings, and splenic pain and enlargement. Pruritus has sometimes proved resistant. Dyspepsia has seemed to be improved, except where ulcers were present. In general all patients are better and most are symptomatically normal. Those who have had other forms of treatment are quite certain that P^{32} is both more effective and much more convenient despite the occasional admission to hospital that is required.

Most symptoms that are continuous, such as facial congestion, headache, dyspnoea, ulceration, and gangrene, are clearly due to the increased blood volume, since they are immediately relieved by an exchange venesection. Pruritus is diminished, but seldom completely, and tends to persist in the palms, especially after a hot bath. It is probably caused in part by the irreversible dilatation of the skin venules. We can draw no conclusions about haemorrhagic episodes, thromboses, and dyspepsia because they are too inconstant. The spleen diminishes slowly only when the P^{32} has had time to act. It became impalpable in 10 of the 27 cases in which it was enlarged.

Commentary on Cases

Group I: Observed for More than One Year.—(A) *Successfully treated* (29 *cases*). Of these, 17 have had more than one treatment. The average length of remission was nearly two years. The longest was four and a half years and the shortest nine months. Of the 12 cases which have had only one treatment the longest remission is three and a half years. (B) *Inadequately treated* (5 *cases*). Two of these were young men with severe and resistant polycythaemia. One has received 36 mC of P^{32} in four years and the other 17 mC in four and a half years. Possibly this dosage was unnecessarily cautious. Two were elderly women who had difficulty in attending regularly. The last was a man of 49 in whom remissions have been short and incomplete for over three years. Although his haemoglobin is now normal he still has a large spleen and a raised blood volume.

Group II: Observed for Less than One Year (7 *cases*).—These cases look like doing well, though it is too soon to be certain.

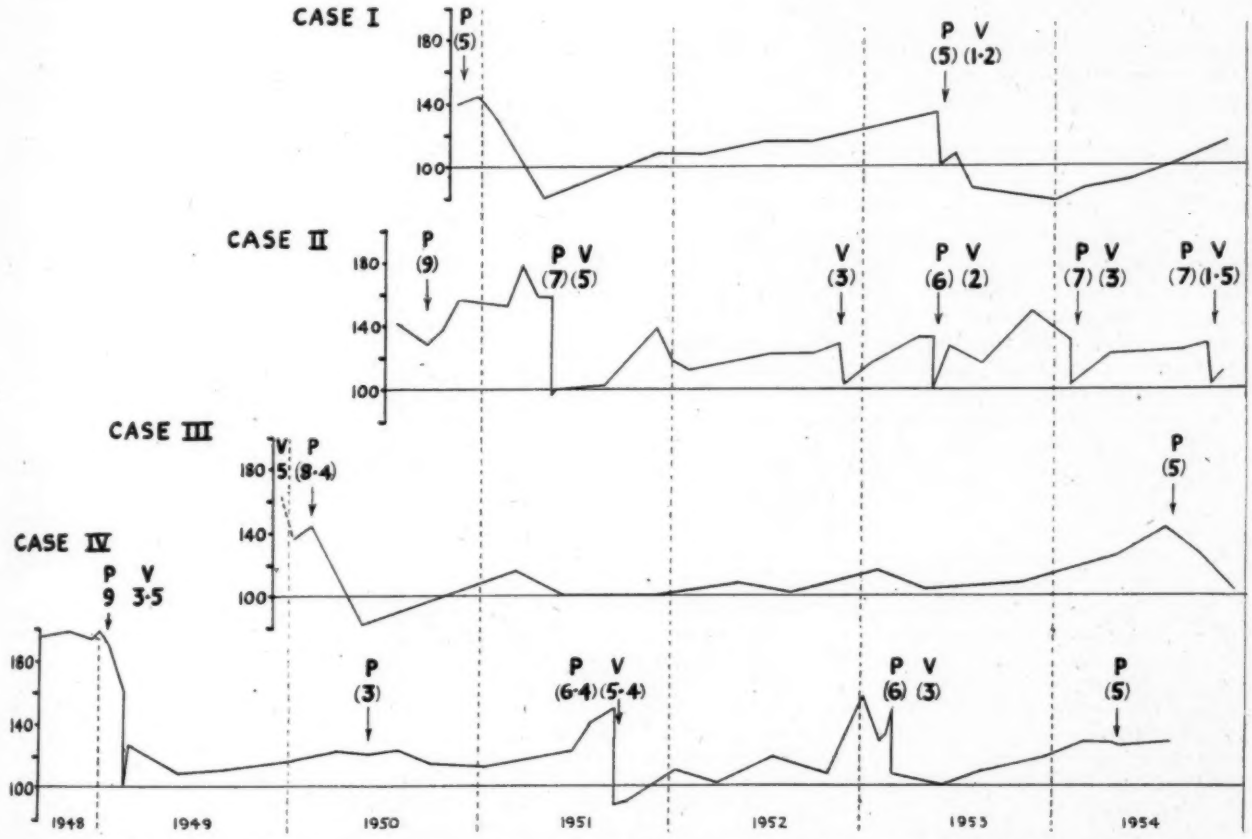
Group III: Dead (4 *cases*).—(1) Female aged 63 with over 10 years' history. Between 1949 and 1953 she was given 20 mC of P^{32} in three episodes with good remissions. After the last she gradually became anaemic and died from acute myeloid leukaemia. (2) Male aged 42. Severe polycythaemia was treated with 13 mC of P^{32}. A year later the patient became anaemic and died, according to reports, from myelosclerosis. (3) Male aged 66. Admitted to hospital with a cerebral thrombosis in 1947. Severe polycythaemia was diagnosed and he was treated by bath irradiation to the trunk (4.2 m.g.r.). In 1948 he was given 4 mC of P^{32} with no effect, and he died elsewhere four years later with polycythaemia. (4) Male aged 77. Diagnosed 1948. Given 7 mC of P^{32} in 1950. Remission for two years was followed by anaemia due to myelofibrosis and haemolysis, of which he died six months later.

Group IV: Insufficiently Followed Up (3 *cases*).—These patients attended too irregularly for any conclusion to be drawn about the effect of treatment.

Summary

A group of 48 patients treated with radioactive phosphorus is described. In severe cases the blood concentration was brought to normal by a massive venesection and simultaneous infusion of plasma substitute.

The presenting symptoms and general course of the disease are reviewed. Observation over a period of up to six years shows that the blood concentration can be kept at or near normal in most cases. When this is done symptoms are relieved. Relief may last from just under one year to over four years, with an average of just under two.



The haemoglobin chart of four illustrative cases. P means the injection of radiophosphorus and the figure in brackets is the dose in millicuries. V means a venesection; the figure is the amount in litres removed, a smaller amount of dextran being replaced.

Case I.—Good control. A woman now aged 68. She is sensitive to small doses of P^{32} (5 and 4 mC). Note that the fall to normal is quicker with venesection and P^{32} than with P^{32} alone. She was out of control in the winter of 1952–3. This is the only case in which the haemoglobin level fell below 100%.

Case II.—Bad control. A man now aged 38. Note the absence of visible effect of 9 mC of P^{32} in 1950. Haemoglobin brought to normal in 1951 by a large venesection, but continues to range around 130% despite subsequent treatments. Total dose of P^{32} was 36 mC and probably should have been more. Nevertheless he is much better for treatment.

Case III.—Good control. A woman now aged 70. Remission of over four years after 8.4 mC of P^{32}, which is the longest we have seen. Note that the haemoglobin did not fall below normal despite the long effect of P^{32}.

Case IV.—Good control. Man now aged 73. A very severe case, but easily treated. The haemoglobin has been kept normal for nearly six years. Note the sudden relapses in 1951 and 1953. The slow rise of haemoglobin in 1954 is of a different type. The small dose of P^{32} in 1950 was possibly unnecessary.

This treatment is quite the most effective and is the least disturbing to the patient.

We would like to thank Professor D. W. Smithers, of the Radiotherapy Department, and Professor W. V. Mayneord, of the Physics Department, and members of their staffs, for making this work possible. We are also grateful to numerous colleagues in this and other hospitals for referring cases to us, and in particular to Dr. P. E. T. Hancock. The earlier cases in the series were treated by Dr. R. J. Walton, to whom we acknowledge our debt.

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PROTHROMBIN AND THE ONE-STAGE PROTHROMBIN TIME*

BY

ARMAND J. QUICK, Ph.D., M.D.

AND

CLARA V. HUSSEY, M.S.

(From the Department of Biochemistry, Marquette University School of Medicine, Milwaukee, Wisconsin)

The discovery that the prolonged prothrombin time of stored human plasma was caused by the disappearance of a clotting factor, hitherto unrecognized (Quick, 1943), made it clear that prothrombin activity depended on more than prothrombin itself and that the one-stage procedure could no longer be regarded unequivocally as a specific test for this constituent. When it was subsequently established that the plasma contained a second prothrombin accessory factor (Alexander *et al.*, 1952), the need for a reinterpretation of the test was further emphasized. It is the purpose of this paper to present pertinent experimental and clinical observations that should be helpful for the re-evaluation of the test, and for furnishing at least a partial answer to several basic questions concerning the prothrombin time.

Methods and Materials

Since the purpose of this study is a critical evaluation of the one-stage prothrombin time, it is necessary to limit discussion to results obtained by the original rigidly standardized method (Quick, 1938). Of particular importance is the source and preparation of the thromboplastic reagent. Rabbit brain carefully cleared of blood and blood vessels and dehydrated with acetone not only has a high and constant activity but is devoid of both stable and labile factors.

In this study blood was collected with a silicone-coated syringe and needle and kept in test-tubes similarly coated. All clotting tests were carried out in uncoated glass test-tubes at 37° C. unless otherwise stated.

Tricalcium-phosphate-treated Plasma.—By means of this adsorbent, prothrombin and stable factor are quantitatively removed, while labile factor and fibrinogen remain unaltered. Since rabbit plasma is exceedingly high in labile factor, it serves as a good source for this agent as well as for fibrinogen. The preparation of the tricalcium phosphate reagent and the procedure for deprothrombinizing plasma have been described in detail (Quick, 1951). Plasma treated with tricalcium phosphate is designated as "$Ca_3(PO_4)_2$ plasma." Stable factor was prepared by the method of Duckert, Koller, and Matter (1953). In many experiments aged serum from normal blood served as the supply of this factor.

Serum Prothrombin Time.—The blood or plasma was clotted in a glass test-tube at 37° C., centrifuged 15 minutes after a solid clot had formed, and reincubated for an additional 45 minutes. The prothrombin time was carried out as follows: 0.1 ml. of fresh rabbit plasma deprothrombinized with $Ca_3(PO_4)_2$ was mixed with 0.1 ml. of 0.02 M $CaCl_2$ and 0.1 ml. of thromboplastin reagent (from rabbit brain). To this mixture 0.1 ml. of the serum was blown in and the clotting-time determined. In this procedure the deprothrombinized rabbit plasma supplies both fibrinogen and stable factor.

Three patients with true congenital hypoprothrombinaemia were available for this study. Two are brothers whose prothrombin times have remained 19 to 26 seconds for the past seven years. The third is a girl whose prothrombin time is 37 seconds. The patients have a normal concentration of labile factor and their prothrombin time is not shortened by stable factor. A patient with pure stable-factor deficiency was also utilized in this investigation. Her prothrombin time varies from 26 to 55 seconds, but is usually about 27 seconds. The addition of stable factor prepared according to Koller completely corrects the prothrombin time. A detailed study of these patients has recently been presented (Quick, Pisciotta, and Hussey, 1955).

For the sake of simplicity the terms "labile" and "stable" (factors) are employed. Labile factor may be considered to be synonymous with factor V or proaccelerin of Owren and ac-globulin of Seegers, while stable factor is probably the same as factor VII of Koller, proconvertin of Owren, S.P.C.A. of Alexander, stable prothrombin conversion factor of Owen, and co-thromboplastin of Mann.

Why is the Prothrombin Time Constant in Fresh Normal Plasma?

Few values of blood are as constant as the prothrombin time. It is consistently 12 seconds in normal subjects, in contrast to the wide variations of prothrombin concentration as measured by the two-stage method, which, according to Mann and his associates (1948), may vary from 244 to 452 units. While it is established that three agents—namely, prothrombin, and stable and labile factors—affect the prothrombin time, it remains to be determined which of these is specifically responsible for the 12-second value of normal blood. A rather convincing answer can be found from the results of Table I. It is to be noted that an excess of neither labile nor stable factor significantly shortens the prothrombin time of fresh normal plasma. After storage in a silicone-treated container for 24 hours, the prothrombin time is increased to 16 seconds. The addition of excess

TABLE I.—*Effect on Prothrombin Time of Adding Excess Labile and Stable Factors to Normal Plasma and Plasma Deficient in These Accessory Agents*

	Prothrombin Time (Seconds)		
	Original	With Excess	
		Labile Factor*	Stable Factor†
Normal plasma	12	12	11½
Stored plasma (labile factor deficient)‡	16	12	16
Plasma deficient in prothrombin	21	21	21
Plasma deficient in stable factor	39	40	12

* To 0.1 ml. of plasma, 0.01 ml. of rabbit plasma deprothrombinized with $Ca_3(PO_4)_2$ was added.
† To 0.1 ml. of plasma, 0.01 ml. of aged serum prepared from normal blood was added.
‡ Stored in a silicone-coated test-tube for 24 hours at 4° C.

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labile factor in the form of deprothrombinized rabbit plasma corrects the prothrombin time to 12 seconds, whereas stable factor has no effect. The addition of labile factor does not correct the prolonged prothrombin time of plasma from a patient with congenital deficiency of stable factor, but a small quantity of aged serum, which has an excess of this factor, brings the value to exactly 12 seconds. Plasma with a prolonged prothrombin time due to a true deficiency of prothrombin is not corrected by an excess of either labile or stable factor.

These results clearly suggest that the concentration of prothrombin fixes the value of the prothrombin time, provided adequate amounts of labile and stable factors are present. Since excess of these accessory factors exerts a corrective effect only on those plasmas which lack the specific factor, it seems clear that a deficiency of any one is not compensated by an excess of the other two. The determinant of the prothrombin time is the component which decreases below a minimal critical level. In normal blood, labile and stable factors are in excess while prothrombin is the limited factor and, therefore, is the agent responsible for the prothrombin time. The constancy of the prothrombin time of fresh normal plasma can therefore be explained by assuming a fixed level of prothrombin.

Why Does the Prothrombin Time Change During Storage?

It is generally accepted that the increase of prothrombin time during storage is caused by a decrease of labile factor. Apparently, the rate of disappearance is related to the calcium-ion concentration, for it is much more when blood is mixed with one-ninth its volume of 0.1 M sodium oxalate or 0.2 M sodium citrate than with 0.1 M sodium citrate. The latter does not completely depress the concentration of ionized calcium and, as seen from the results recorded in Table II, no demonstrable amount of labile factor is lost in

TABLE II.—*Changes in Prothrombin Activity of Normal, Prothrombin-deficient, and Stable-factor-deficient Blood During Storage*

	Immediate	After 24 Hours' Storage	
		In Glass	In Silicone
Normal blood (9 volumes) and sodium oxalate 0·1 M (1 volume)	12	15	16
After adding labile factor ..	12	8	12
" " stable " ..	11½	15	16
Normal blood (9 volumes) and sodium citrate 0·1 M (1 volume)	12	9	12
After adding labile factor ..	12	8	12
" " stable " ..	11½	9	12
Prothrombin-deficient blood (9 volumes) and sodium oxalate 0·1 M (1 volume)	23	37	39
After adding labile factor ..	23	17	23
" " stable " ..	23	37	39
Stable-factor-deficient blood (9 volumes) and sodium oxalate 0·1 M (1 volume)	39	30	33
After adding labile factor ..	40	25	30
" " stable " ..	12	18	18
" " labile and stable factor	11½	9	12

24 hours. Significantly, with this anticoagulant no change in the prothrombin time occurs if the plasma is stored in a silicone-coated tube, but a marked decrease is observed when stored in glass. This rise in prothrombin activity can be explained either by an actual increase in prothrombin or by the generation of an accelerator. Irrespective of which explanation is correct, it is obvious that storage in glass increases prothrombin activity as measured by the one-stage test. Owing to the simultaneous decrease in labile factor, the increase in activity is usually masked. Thus the prothrombin time of oxalated plasma after 24 hours' storage in glass is 15 seconds, but when labile factor is added it decreases to 8 seconds. The plasma in the silicone-coated test-tube has nearly the same prolonged prothrombin time, but labile factor reduces it only to 12 seconds. This suggests that the generation of prothrombin activity is slower in silicone than in glass.

When oxalated plasma deficient in stable factor is stored the prothrombin time is further increased in both glass and silicone. If labile factor is added, a partial correction occurs, whereas the addition of stable factor caused no shortening. When both labile and stable factors are added the prothrombin time is reduced to 8 or 9 seconds. Plasma from a patient with true hypoprothrombinaemia likewise, when stored, exhibits a further prolongation of the prothrombin time which is partly corrected by the addition of labile factor. Stable factor has no corrective action.

From these results one may conclude that if the increase in the prothrombin activity of stored plasma is caused by the generation of an accelerator, it is produced independently of either labile or stable factors. It is significant that plasma which lacks prothrombin shows only a small increase in activity on storage and that neither stable nor labile factors bring the prothrombin time to normal. Two basic causes account for changes in the prothrombin time of stored plasma: the first is a loss of labile factor, the second is either an actual increase of prothrombin or the generation of an accelerator independent of either labile or stable factors. In the absence of labile factor the increase of this prothrombin activity is masked.

Why is the Prothrombin Time of Serum from Haemophilic or Thrombocytopenic Blood Shorter Than That of Plasma?

When plasma deprived of platelets by means of high centrifugation or obtained from subjects having thrombocytopenia or haemophilia is clotted in glass, the serum has a prothrombin time of 8 seconds provided the plasma is normal —that is, gives a value of 12 seconds (Table III). It is certain that the poor consumption of prothrombin explains in

TABLE III.—*Prothrombin Time of Plasma and Its Corresponding Serum in Haemophilia and Thrombocytopenia*

Type of Plasma	Platelet Count	Prothrombin Time		
		Of Plasma	Of Serum	Of Stored Plasma with Labile Factor Added
		Sec.	Sec.	Sec.
Haemophilic	300,000	12	8	8
Thrombocytopenic	65,000	12	9½	8
Normal (highly centrifuged) ..	3,000	12	8	8
Hypoprothrombinaemic (congenital)	270,000	20	180+	16
Congenital hypoprothrombinaemia (highly centrifuged) ..	3,500	20	20	16
Stable factor deficient ..	250,000	27½	73	18½
" " " (highly centrifuged)	3,000	27½	19	18½

part the short prothrombin time, but does not account for a value of 4 seconds less than that of the fresh plasma. Since the same decrease occurs in plasma stored in glass to which excess labile factor is added, one may conclude that a common mechanism is responsible for the increased prothrombin activity. As already stated, the most obvious explanation is either an actual increase in prothrombin or the generation of an accelerator.

When one compares the prothrombin time of the serum obtained from normal blood with that of blood from a patient with true hypoprothrombinaemia, one finds that the serum prothrombin becomes extremely prolonged in the latter and only to 20 seconds in the particular normal blood used in this experiment. When blood from the hypoprothrombinaemic patient is highly centrifuged and the resulting plasma clotted, the serum has about the same prothrombin time as the serum, thus suggesting that either little new prothrombin is formed or little accelerator is generated.

The results obtained on blood lacking stable factor are particularly interesting. With an adequate supply of platelets the consumption of prothrombin as measured by the serum prothrombin time is fairly high, indicating that

deficiency of stable factor does not prevent normal utilization of prothrombin. When stable factor is added in determining the prothrombin time of the serum a value lowered to normal is obtained, thus showing that the serum does not contain adequate amounts of the factor to assure an accurate prothrombin time. Even more striking are the results when the stable-factor-deficient and platelet-poor plasma is clotted. The serum shows a prothrombin time less than that of the plasma but still markedly prolonged. The addition of stable factor brings the prothrombin time to 9 seconds. Since the addition of a fixed amount of stable factor corrects the prothrombin time of the fresh plasma from the patient with pure stable-factor deficiency to 12 seconds and the serum from the platelet-poor plasma to 9 seconds, it is obvious that these two values are not fixed by the stable factor. The results obtained on the serum from true hypoprothrombinaemic plasma suggest that the serum prothrombin time is closely related to the prothrombin concentration.

The answer to the question heading this discussion is : The prothrombin time of serum from haemophilic or thrombocytopenic blood is shorter than that of the corresponding plasma because almost no prothrombin is consumed and, in addition, there is formed either additional prothrombin or an accelerator independent of labile or stable factors.

Why is the Prothrombin Time of Blood of Newborn Babies Normal When Measured by the One-stage Method and Low by the Two-stage Procedure?

If it is possible to answer this question satisfactorily a real advance should be made in clearing the confusion concerning the interrelationship of prothrombin and accelerators. The original study of Brinkhous, Smith, and Warner (1937) established that the prothrombin is only about 30% as high in newborn as in adult blood. Equally as incontrovertible is the fact that the prothrombin time is 12 seconds in almost all newborn infants whose mothers had adequate amounts of vitamin K (Quick, Murat, Hussey, and Burgess, 1952). Warner, Brinkhous, and Smith (1939) explained this difference by postulating a change in convertibility of prothrombin. Later, the discovery of the labile and stable factors made it appear probable that these accessory factors might in some way be accountable for this striking discrepancy. The finding that the labile factor is normal in newborn blood (Quick, Flood, and Hussey, 1953; Owen and Hurn, 1953) eliminates this agent from consideration. The report of Loeliger and Koller (1952) that the stable factor is reduced in newborn blood clearly shows that it cannot be the agent that compensated for the lack of prothrombin and thereby normalizes the prothrombin time.

The results of a few simple experiments recorded in Table IV offer pertinent information. While the prothrombin time of newborn plasma is 12 seconds, which is the same as that of adult plasma, it fails to show the characteristic shortening of the latter on storage. Likewise, the prothrombin time of serum prepared from platelet-poor newborn plasma is not 8 seconds, as is the serum from platelet-poor adult plasma, but is 12 seconds, which is the same as the original plasma.

TABLE IV.—*Comparison of Prothrombin Activity in Adult and in Newborn Blood*

	Prothrombin Time	
	Adult	Newborn
1. Fresh plasma	12 sec.	12 sec.
2. Stored plasma*	9 ,,	12 ,,
3. Serum from platelet-poor plasma	8 ,,	12 ,,
4. Plasma diluted with equal volume of saline	15 ,,	15 ,,
5. Plasma diluted with equal volume of $Ca_3(PO_4)_2$-treated plasma	12 ,,	15 ,,

* In glass at 4° C. for 24 hours with 0·1 M sodium citrate.

Earlier it was pointed out that the increase in prothrombin activity of adult plasma on storage or in serum from platelet-poor plasma could be explained by postulating either an actual increase in prothrombin or by the evolution of an accelerator. From the results obtained on newborn plasma it is clear why the first is the more likely explanation. According to the two-stage test, the prothrombin of newborn blood is only about one-third of that in adult blood. Since no evidence of an accelerator in newborn blood has been demonstrated, it seems quite plausible that the augmented prothrombin activity in adult blood is caused by an actual increase in prothrombin derived from an inactive precursor that may be designated as prothrombinogen. According to this hypothesis, newborn blood lacks this precursor, and this accounts for the low prothrombin obtained with the two-stage method. The one-stage method specifically measures active prothrombin and is unaffected by prothrombinogen.

Further support for the concept is obtained from the results of experiments 4 and 5 of Table IV. If either newborn or adult oxalated plasma is diluted with an equal volume of saline the prothrombin time is increased to 15 seconds. If, however, plasma treated with $Ca_3(PO_4)_2$ is used as the diluent, the prothrombin time of adult plasma remains 12 seconds, whereas that of the diluted newborn plasma is 15 seconds. Apparently, $Ca_3(PO_4)_2$-treated plasma contains a factor which can convert inactive prothrombin to the active state. Since newborn plasma is devoid of prothrombinogen, the addition of the deprothrombinized plasma cannot increase the active prothrombin, and therefore the prothrombin time becomes prolonged to 15 seconds, the same as is obtained by dilution with saline.

To present the hypothesis in an easily comprehensible form one may visualize prothrombinogen as prothrombin kept inactive by an inhibitor, "X." On storage the inhibitor deteriorates, thus liberating prothrombin, which accounts for the increased prothrombin activity. Plasma treated with $Ca_3(PO_4)_2$ contains an agent which can activate prothrombinogen presumably by removing the inhibitor. If the factor be designated "Y" one can postulate an equilibrium according to the following equation :

$$\underset{\text{(prothrombinogen)}}{\text{Prothrombin X}} + \text{Y} \rightleftharpoons \text{Prothrombin} + \text{XY}$$

This is undoubtedly an oversimplification, but the essential idea offers a logical answer to the four basic questions presented. It appears to be the Y factor which fixes the level of free prothrombin in human blood, and therefore it is the basic determinant of the prothrombin time. There is evidence that the concentration of this agent is determined by heredity. A family has been reported in which a mother and two of her children have a prothrombin time of 16 minutes, due presumably to a lower-fixed concentration of factor Y (Quick, Flood, and Hussey, 1953).

According to the present findings, the answer to this fourth question is : The newborn plasma has a normal prothrombin time because it has a normal concentration of free prothrombin, but it has a lower prothrombin as measured by the two-stage method because it is devoid of prothrombinogen. Its total prothrombin content which the latter test measures is much lower than in adult blood.

Relation of Haemorrhage to Prothrombin Time

In the early study of poisoning from spoiled sweet clover hay it was observed that a heart puncture caused fatal haemopericardium whenever the rabbit's prothrombin time was markedly prolonged (Quick, 1937). Later it was shown that a puncture caused fatal bleeding when the prothrombin time was 24 seconds or longer (Quick, Honorato, and Stefanini, 1948). Interestingly enough, these findings correspond remarkably well with human findings. Two boys who have a prothrombin time varying from 19 to 26 seconds due to congenital true hypoprothrombinaemia have a rather mild but distinct bleeding tendency. A girl of another family who has a more severe deficiency of prothrombin, with a prothrombin time of 35 seconds, has a much more severe bleeding condition. A woman aged 50 who has a prothrombin time which varies from 27 to 51 seconds due to a pure deficiency of stable factor has a rather mild bleeding history.

The exact relation of the prothrombin time to haemorrhage in the human is difficult to determine. In most types

of coagulation defect bleeding does not occur unless induced by trauma. Even a severe haemophiliac with a clotting-time over one hour may have no bleeding episodes for long periods. Since the newborn infant with a normal prothrombin time but a low prothrombin as measured by the two-stage method can undergo surgery with impunity, one can conclude that the one-stage method is the more reliable in that it measures the fraction of prothrombin that apparently participates directly in haemostasis.

Discussion

A hypothesis has been offered to help answer four basic questions concerning the prothrombin time. The central idea is that the prothrombin in adult blood is present partly in the active form and partly as prothrombinogen. The one-stage method measures only the active prothrombin, while the two-stage test determines total prothrombin—that is, both the active and the inactive fractions. The early studies of Bordet (1919) already indicated the possibility of inactive prothrombin. He concluded that all of the prothrombin was in the precursor state, to which he gave the name proserozyme. The concept of Warner *et al.* (1939) of an altered convertibility of prothrombin is in accord with the basic concept provided one reinterprets convertibility. It is unlikely that the prothrombin molecule can have gradations of convertibility. There is a much greater probability that the convertibility follows the all-or-none law. It is either entirely non-convertible—that is, in an inactive state—or fully convertible, and the apparent convertibility actually is the ratio of free to total prothrombin. The higher the percentage of free prothrombin, the greater will appear to be the convertibility.

Whether the hypothesis is accepted or not, it must be recognized that the prothrombin time of plasma is easily altered by relatively simple factors such as contact with glass. Any modification of the original procedure is apt to measure something different from what is present in the plasma immediately after removal from the vein. Modifications designed to measure prothrombin specifically deserve particular scrutiny. Contrary to the claims that the prothrombin time is not a measure of prothrombin, it can be argued from the evidence presented in this paper that it is actually the only method which determines active prothrombin. It is to be emphasized that the one-stage and two-stage methods do not measure the same thing in human blood, and therefore there is no justification to use the two-stage procedure as the criterion to evaluate the one-stage test. Since deficiency of stable and labile factor can easily be detected and the test corrected accordingly, the one-stage method continues to remain the simplest and probably the most reliable means to determine prothrombin.

Summary

In this study evidence is offered to show that the constancy of the prothrombin time of fresh normal human plasma is due to the fixed concentration of active prothrombin. The increase of prothrombin activity during storage and during the clotting of haemophilic or platelet-poor plasma can be explained simply by the assumption that adult blood contains in addition to active prothrombin a high concentration of inactive prothrombin (prothrombinogen) which does not influence the one-stage method but is measured by the two-stage test. During storage or clotting the precursor is converted to active prothrombin, which in the hypothromboplastic states is not consumed and therefore accumulates. Newborn blood contains a normal concentration of active prothrombin but is devoid of prothrombinogen, which accounts for the normal prothrombin time but the low prothrombin as measured by the two-stage test.

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CARDIAC GLYCOSIDES IN THE TREATMENT OF CARDIOGENIC SHOCK

BY

RICHARD GORLIN, M.D.
Chief Medical Resident, Peter Bent Brigham Hospital, 1953–4

AND

EUGENE D. ROBIN, M.D.
Chief Medical Resident, Peter Bent Brigham Hospital, 1954–5

From the Medical Clinics, Peter Bent Brigham Hospital, and the Department of Medicine, Harvard Medical School

Myocardial infarction complicated by severe shock is usually attended by a mortality estimated as high as 93% (Rosenbaum and Levine, 1941). Numerous forms of therapy have been advocated for this serious complication, including vasopressor agents, transfusions, and cardiac glycosides (Hellerstein and Brofman, 1951). The use of the first two agents has been fairly well clarified in the past five years, but the role of cardiac glycosides, in the absence of overt or predominant congestive failure, is as yet unsettled.

Four cases are presented to illustrate the specific use of the cardiac glycosides in the treatment of cardiogenic shock, and in so doing to demonstrate survival from the usually lethal combination of pulmonary oedema and shock.

Case 1

A 60-year-old undigitalized hypertensive man entered hospital in shock. He had had a previous myocardial infarction four years prior to admission. He collapsed on the morning before admission and was found to be cold, sweaty, cyanotic, and unresponsive. No blood pressure was obtainable. There were bilateral moist rales up to the scapulae. An electrocardiogram showed an acute posterior myocardial infarction with bizarre arrhythmias, including ventricular tachycardia, ventricular bigeminy, and auricular flutter. He was given 50 mg. of procaine amide hydrochloride ("pronestyl") intravenously, with conversion to a normal sinus mechanism. Treatment with intravenous noradrenaline raised the blood pressure to 100/80, but he remained unresponsive and in clinical shock. Slowing of the infusion resulted in an immediate fall in blood pressure. He was then given 0.4 mg. of lanatoside C intravenously. Thirty minutes later the heart sounds became more distinct, and he was able to speak and recognize his family. Blood pressure was maintained without vasopressors. Signs of congestion virtually

disappeared. He was given another 0.4 mg. of lanatoside C and appeared to be doing well. Approximately one hour after this dose he suddenly died. A pre-terminal electrocardiogram showed ventricular fibrillation. Post-mortem examination showed a fresh posterior myocardial infarction and pulmonary congestion.

Comment.—Shock and coma responded specifically to lanatoside C. Blood pressure was maintained without vasopressors. Death may have been related to a digitalis-induced arrhythmia.

Case 2

A 49-year-old white woman with disseminated lupus erythematosus had been on cortisone, 75 mg. daily, and had had severe hypertension, congestive heart failure, and angina pectoris. She was maintained on digitalis, 0.1 g. daily, but this had been omitted two days before admission. Five hours before admission she developed left anterior chest pain followed by acute dyspnoea and cyanosis. On admission to hospital she was found to have rales to the apices and gurgling respirations. The blood pressure was 250/138, pulse 152, respirations 40. An electrocardiogram showed left ventricular hypertrophy and a possible anteroseptal myocardial infarction.

The patient was treated initially with morphine, 10 mg., atropine, tourniquets, and a 250-ml. venesection, with a fall in blood pressure to 110 systolic. Pressure was maintained at this minimum level with phenylephrine hydrochloride ("neosynephrine") intravenously in 5–15-mg. doses. When the blood pressure was at its peak of 110 systolic the pulmonary oedema became worse; however, when the blood pressure became less than 90 the pulmonary oedema lessened, but the patient became unresponsive. As the hours wore on she remained in coma and pulmonary oedema at all blood-pressure levels. The pulse rate was 135 and the blood pressure could not be maintained above 100 mm. Hg. At this time ouabain was given intravenously in divided doses of 0.05 mg., to a total of 0.15 mg. Forty-five minutes after initiation of this therapy three things occurred: the patient awakened and became alert, the blood pressure was easily maintained at any level on phenylephrine, and despite the blood pressure being maintained at about 120 to 130 mm. pulmonary oedema cleared.

Comment.—In this patient shock and coma were successfully treated with ouabain. Vasopressor action was aided and supported by digitalization.

Case 3

A 65-year-old widowed white woman had had a known hypertension of 160/100, angina pectoris, and probably myocardial infarctions for fourteen months before admission. Twenty-four hours before admission she developed severe substernal pain with radiation down the left arm and sweating. These disappeared only to recur four hours before admission, and were associated with progressively severe dyspnoea and later with orthopnoea and cyanosis. The patient entered the emergency ward, where her blood pressure was 190/110, pulse 150, and respirations 40. She was cyanotic, foaming at the mouth, the veins were full, and rales were heard to the apices. A diastolic gallop and pulsus alternans were present.

Oxygen, 15 mg. of morphine sulphate intravenously, and a 300-ml. phlebotomy was given. On this treatment respirations were noted to be less laboured. However, about half an hour later the blood pressure fell to 100/80 with disappearance of peripheral pulses and she lapsed into coma. She appeared to be in clinical shock at this time. Thereupon 0.2 mg. of ouabain was given intravenously. The pulse rate dropped from 150 to 120 in 15 minutes and the pulse became strong. The blood pressure rose to 125/80 and she awakened. Half an hour after the administration of ouabain she had transient multi-focal ventricular premature beats, treated successfully with 250 mg. of procaine amide hydrochloride intramuscularly. She gradually recovered. An electrocardiogram showed left ventricular hypertrophy and an anteroseptal infarct of uncertain duration. The sedimentation rate, white blood count, and blood sugar rose early with a fall in all three after the first two weeks, substantiating the clinical impression of myocardial infarction.

Comment.—This patient with shock and pulmonary oedema responded dramatically to digitalization. The dramatic clinical improvement probably cannot be attributed to the fall in heart rate from 150 to 120 because in the absence of mitral stenosis such a rate is seldom critical. The equivocal electrocardiogram is probably caused by the two prior infarctions.

Case 4

A 68-year-old white woman had been having exertional dyspnoea, chest pain, and paroxysmal nocturnal dyspnoea for two months. She was brought to hospital unconscious and slightly cyanotic. The skin was clammy and cool; blood pressure 280/140; pulse rate 130; respiratory rate 32. She had not been digitalized. There were rales to the apices and the veins were full. An electrocardiogram showed an anteroseptal infarct and auricular flutter. She was treated with oxygen, 10 mg. of morphine sulphate, and venesection without effect. The blood pressure fell to 120/70 and the typical picture of shock developed. Then 0.125 mg. of ouabain was given intravenously; in 20 minutes she was awake, with clearing of her chest and stabilization of blood pressure at 160/80 and a heart rate of 110. She was discharged four weeks later.

Comment

Herrick (1912), in his classic article on the subject, recommended the routine use of digitalis in myocardial infarction. Within the last 25 years, however, clinicians have been hesitant to use digitalis in myocardial infarction because (1) the tolerance of the experimentally infarcted heart to digitalis is decreased (Travell *et al.*, 1938), and (2) both digitalis and myocardial infarction increase the likelihood of ventricular irritability and arrhythmia, and their effects may be additive in the same patient (Goodman and Gilman, 1941). In 1951 Askey gave digitalis to half of a group of 100 patients with proved myocardial infarction. He failed to show any increased incidence of arrhythmia or sudden death in the digitalis-treated group. In fact, Gilson and Schemm (1950) administered digitalis for its classical contraindication—namely, ventricular tachycardia—with salutary results in four patients.

There appears to be general agreement regarding the use of cardiac glycosides for frank congestive failure complicating cardiac infarction, but whether these agents have any role in treating the shock of cardiac origin is less certain. Goodman and Gilman (1941) take a strong position in opposing its use as follows: "Digitalis is contraindicated during the first few days following an acute coronary thrombosis. *The clinical picture is usually one of shock rather than congestive heart failure, and digitalis, by further decreasing cardiac output, may make the patient worse.*"

Recent haemodynamic studies have contributed much to an understanding of this problem. Clinical shock implies that the blood pressure in the arterial tree is much less than normal. The level of the blood pressure depends on the height of systemic resistance—that is, vasoconstriction or dilatation—and the level of the cardiac output. Either the resistance or the cardiac output is low when there is shock. It is only in a small group of patients that a low systemic resistance is seen. G. Lee (personal communication) has demonstrated in some patients with the severe pain of an infarction that there may occur a marked muscle vasodilatation with a concomitant normal cardiac output and resulting fall in blood pressure. Most patients, however, show vasoconstriction with an increased systemic resistance and a decreased cardiac output (Freis *et al.*, 1952).

The lowered blood pressure indicates either inadequate, although increased, constriction or a greatly depressed cardiac output, out of proportion to homoeostatic compensation. This decrease in output is related either directly to the myocardium itself or to poor venous return consequent

upon decreased venomotor and muscle pump activity. This latter is seen in nitrite syncope and spinal anaesthesia. However, this possibility seems less likely because shock often exists in the presence of an elevated venous pressure, and the simple restoration of venous pressure by either position in bed or intravenous infusion is not usually effective. The decreased output, then, is probably the direct result of a decreased myocardial contractility (Corday *et al.*, 1949) with the consequent immediately limited ability of the heart to do work following myocardial infarction. The ultimate response of the heart will, of course, depend on the size of the area of infarction and ischaemia, although small infarcts may in and of themselves initiate shock. The whole pattern is a vicious cycle in that the low perfusion pressure occasioned by the myocardium results in poor coronary inflow, with further myocardial ischaemia and hypodynamic myocardial contraction (Wiggers, 1923).

Why the systemic resistance is not maximally increased is not clearly understood. Whether there is a vasomotor paralysis with poor cerebral flow is not known, but in this regard cardiogenic shock is similar to traumatic shock. The first line of defence, then, is to further increase this systemic resistance and decrease the vascular bed to be perfused. The second line of defence is to increase the stroke work of the heart and hence perfusion pressure and minute output. Here has rested the controversy.

Harrison (1939) was among the first to call the shock of coronary thrombosis forward failure and thus semantically implicate the myocardium itself. Stead and Ebert (1942) reported six cases of myocardial infarction resulting in shock. One patient received ouabain and there was an increase in the blood pressure, although the patient subsequently died. Boyer (1944) stated that the shock and the pulmonary oedema syndromes were simply different stages of the same myocardial insult, and perhaps digitalis should be used in both conditions. Fink *et al.* (1953) described the cases of 10 patients in varying degrees of shock who had received lanatoside C. Their criterion for the use of this agent was an elevated venous pressure, suggesting that in such cases shock was myocardial in origin. In every case, despite the ultimate outcome, the blood pressure rose following digitalis administration while the venous pressure was variably affected. It is noteworthy that three of their patients had nearly normal venous pressure and still showed improvement in arterial blood pressure.

Lee (personal communication) demonstrated the fallacy of accepting normal venous pressure as an index of minimal right ventricular failure in patients with myocardial infarction. Although the venous pressure was normal, the gradient between veins and right atrium had disappeared and the right atrial pressure was higher than normal. Finally, studies by Sarnoff *et al.* (1954) have shown that the production of simple haemorrhagic shock in normal dogs results in elevation of left atrial pressure, while right atrial pressure is normal. These experimental observations fit well with the clinical fact that many patients with myocardial infarction have normal venous pressures, yet show pulmonary congestion first by *x*-ray examination and finally at necropsy (Friedberg, 1950).

Our own clinical reports support the above-presented evidence. The effect of the cardiac glycosides is not only to improve the stroke output of the heart but to increase its ability to deliver the blood against the increased peripheral resistance. The first patient demonstrated clearly that a normal arterial pressure could be maintained solely by digitalis. The second patient demonstrated that increased blood pressure could be delivered by the heart when digitalized optimally, and that this could be done without the production of pulmonary oedema. Similarly, shock was averted solely by the use of ouabain in two patients who had the combination of shock and pulmonary oedema. It is particularly noteworthy that all four patients had been in coma as well as shock; two received vasopressors without effect, yet came out of coma without change in blood pressure following cardiac glycoside, and one patient no longer had pulmonary oedema yet maintained an increased arterial pressure. This suggested that cerebral and coronary blood flows were probably increased.

This is not to propose the standard use of the cardiac glycosides in myocardial infarction, but rather to re-emphasize that so-called cardiogenic shock is a manifestation of forward failure. Clinical methods of defining failure of the left ventricle are poor, and the right ventricle seldom manifests gross failure early in acute myocardial infarction. Finally, patients not previously in failure and with normal blood volumes may not develop massive right-sided congestion. Because overt evidence of failure is frequently absent, therapy in this type of shock is seldom aimed at the heart itself.

It is recommended that an orderly therapeutic problem might include the following: (1) morphine sulphate for pain; (2) position in bed for its effect on blood pressure and venous return; (3) phlebotomy for elevated venous pressure; (4) vasoconstrictor agents for increasing systemic resistance and arterial pressure; and (5) cardiac glycosides for increasing stroke work and with it cardiac output and arterial pressure. Each should be tried in additive succession—realizing the physiological contribution of each agent—that is, how digitalis may support the pressor response to phenylephrine hydrochloride as in Case 2. Digitalis is still a potentially dangerous drug and should be used only when the indications are clear cut. The dose is important in avoiding acute toxicity. We achieved therapeutic responses with 25–50% of the generally accepted effective dose of ouabain (Friedberg, 1950). The first patient may have died in a fashion temporally related to digitalis intoxication, and the third patient developed premature bigeminal beats thirty minutes after a remarkable therapeutic effect had been achieved. We recommend small doses of intravenous glycoside. Ouabain has not been a dangerous agent in our hands because we have used 0.05, 0.1, or 0.2 mg. as initial doses instead of the recommended 0.5 mg., and similar aliquots of other intravenous preparations.

Conclusions

Four patients, one in clinical shock and three with shock and pulmonary oedema, were treated primarily with a cardiac glycoside intravenously in small doses. All four patients showed remarkable clinical response, with a rise in blood pressure, decrease in pulmonary oedema, and dramatic clearing of coma. Three of the four ultimately survived. It is re-emphasized that the shock of myocardial infarction represents true myocardial failure and that the use of digitalis may be highly efficacious. When given, digitalis should be administered in doses fractionally 25–50% of the initial dose given to the average cardiac patient. In so doing many of the toxic complications may be avoided.

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LYMPHANGIOGRAPHY

A TECHNIQUE FOR ITS CLINICAL USE IN THE LOWER LIMB

BY

J. B. KINMONTH, M.S., F.R.C.S.
Professor of Surgery, St. Thomas's Hospital

G. W. TAYLOR, F.R.C.S.
B.M.A. Walter Dixon Research Scholar; First Assistant, Surgical Professorial Unit, St. Bartholomew's Hospital

AND

R. KEMP HARPER, M.D., F.R.C.P.Ed., F.F.R.
Director, Department of Radiology, St. Bartholomew's Hospital

Arteriography and phlebography have been used in clinical medicine since their development some twenty years ago. The early work with these techniques was done by dos Santos *et al.* in 1931, Moniz *et al.* (1932), and dos Santos (1938). A comparable method of studying the lymphatic circulation would be of obvious value, but its development has been delayed by technical difficulties. Lymph vessels, or at least normal ones, are much smaller than the arteries or veins used in angiography. They contain colourless lymph, which makes them difficult to see, and under normal circumstances they may be empty or nearly so, existing as potential spaces like the pleura or peritoneum (Kinmonth, 1952). Special methods have therefore been developed to make the lymph trunks visible to the naked eye at operation and opaque to *x* rays so that radiographs could be made to study their role in disease in man. Some of our findings have already been described (Kinmonth, 1951, 1952, 1954; Kinmonth and Taylor, 1954). This paper describes a method which has proved useful in practice and which embodies certain technical improvements. The general principle is that the lymph trunks are made visible to the naked eye by subcutaneous injection of a diffusible blue dye so that radio-opaque solution can be injected direct into them through a small needle.

Lymphangiography of the Leg and Thigh

(1) The diffusible dye patent blue* (also known as patent blue violet or patent blue V) is made up into an isotonic solution (11%) in distilled water and sterilized by autoclaving. About 2 to 2.5 ml. of this solution is injected subcutaneously between the toes, roughly 0.5 ml. into each web, which is massaged with gauze for about half a minute.

(2) The ankle-, knee-, and hip-joints are then passively moved repeatedly through their full range for five minutes. The dye, which permeates the lymph trunks soon after injection, is thus moved along them so that they are filled as far as the pelvis. In this dosage (up to 2.5 ml. for an adult) the dye is without toxic effects. It is, however, absorbed into the blood stream, and the patient soon becomes blue in colour. The anaesthetist and the nursing staff in the ward are warned of this. It is excreted in the urine, and the patient regains a normal complexion in about 24 hours. Severe oedema of the limb should be reduced so far as is possible by elevation and massage for a few days beforehand, because the flow of dye through the lymph trunks may be retarded if they are waterlogged by tissue fluid.

*Obtainable from G. T. Gurr, 36, New King's Road, London, S.W.6.

(3) A bloodless field is helpful in the next stage. This can be produced with a rubber bandage and air cuff, but a better way is to tilt the patient into a full Trendelenburg position so that the limb is sharply elevated.

(4) A transverse incision is made in the skin of the dorsum of the foot about 2 in. (5 cm.) proximal to the webs of the toes (Fig. 1). The lymph trunks run upwards in the line of the long axis of the foot, and it is sometimes possible to see them filled with the blue dye through the skin before the incision is begun. They lie very close to the skin, which is thin in this situation, and so the incision must be deepened by cautious light strokes of the scalpel.

FIG. 1.—Injection of diodone into a lymphatic (see description in text).

Small bleeding points are coagulated with the diathermy. Lymph trunks of normal size are just under 1 mm. in diameter. A length of some 5 or 6 mm. is exposed by gently pushing apart the edges of the incision with the scalpel. A clean exposure of the superficial aspect of the vessel is necessary, but its whole circumference must not be free or it may collapse and make injection impossible.

(5) At this stage it is helpful to distend the lymph trunk with dye. An assistant places a finger on the skin an inch (2.5 cm.) above the incision, and presses gently to obstruct the lymph trunk, and the surgeon massages the interdigital area so that the dye passes up and fills the exposed length. The exposed length of lymphatic is held as straight as possible by grasping the areolar tissue next to it in the distal part of the incision. All is now ready for the injection.

(6) The radio-opaque solution used is 70% diodone. The preparation known as "pyelosil" has given good results in our experiments. It has been kept warm until required, when a 10-ml. syringe is filled with it. A No. 18 hypodermic needle is firmly mounted on the syringe. This is the smallest needle of the standard sizes and its bore will just allow the viscous solution to pass. The needle point is introduced some 2 mm. into the lymph trunk and the piston tentatively advanced. If it is accurately placed, diodone enters and the vessel becomes white and transparent. If, however, the needle point lies in adventitia a bleb forms and the injection must be stopped and another attempt made, often in another reach of the lymphatic or in another vessel. If all is going well the injection is continued, the surgeon watching the needle-point and an assistant telling him of the progress of the piston along the barrel of the syringe. The diodone is injected as rapidly as the small bore of the needle will allow. The full 10 ml. is injected if possible, but sometimes rapid extravasation around the needle occurs before this and the injection is then stopped. Surprisingly good delineation is sometimes obtained with injections as small as 1 ml. Minor leakage of diodone around the needle during the injection is gently mopped up with cut pieces of gauze by an assistant, who takes care not to disturb the needle point.

(7) The needle is withdrawn when the injection is complete and the table immediately altered from the Trendelenburg to the horizontal position.

(8) The *x*-ray tube is moved into position and radiographs are made of the whole limb with as little delay as possible. The sooner they are made the better will be the definition, because the diodone starts to diffuse through the permeable walls of the lymphatics after a few minutes, giving rise to blurred outlines in the film. The films have been placed in position under the limb in the beginning so that no time is lost at this stage.

Radiological Technique

As with all radiographic procedures in operating theatres, radiography in these cases is carried out under certain difficulties. Examination is even more difficult when the thicker parts of the body such as the pelvis, abdomen, and thorax have to be radiographed.

FIG. 2. — Normal lymphangiogram: 6 ml. of 70% diodone was injected and the films were exposed one minute later.

FIG. 3.—Lymphangiogram in a patient with idiopathic lymphoedema: 10 ml. of 70% diodone was injected and the films were exposed one and a half minutes later.

Good definition and reasonable contrast are essential, as normal lymphatics are demonstrated as fine opaque filaments in the soft tissues.

It has been found advantageous to use non-screen film for the extremities and screened films for the thicker parts. Exposure times need not be as critical as in arteriography, as the flow of opaque medium through the lymphatics is comparatively slow, but immobilization is essential, and undue delay may result in blurred lymphatic outlines, due to seepage through the walls of the vessels.

The films or cassettes are placed in boxes, under the sterile towels, below the part to be examined and prior to the injection. Several non-screen films can be used if necessary, each protected from the other by lead-protected trays, the box being long enough to carry on each tray two 15 × 6-inch (38 × 15-cm.) films placed end to end. There is no appreciable gap between the end-to-end films, so that little of the lymphatic system is undemonstrated. Almost the whole length of a limb can be radiographed at one time with a special type of tube arm which we use on these mobile units to give adequate focus–film distance. The trays are removed one by one from the distal end of the box as each exposure is made.

In general, it is unnecessary to take serial films of each area (such as are required in arteriography) unless more of the lymphatic system has to be filled by a further injection. It is of great advantage to have a wedge filter to compensate for the varying thickness of the lower limb, and the recent use of such an accessory, similar to that which we use in arteriography, has been of much value in improving the quality of the films. A difficulty may be to make interchange of the filter simple, as it is not always practicable to have the same mobile *x*-ray set available for this type of operating-theatre work.

A cassette and a fixed grid, usually in a cassette tunnel, are used for the successful demonstration of the inguinal glands and pelvic lymphatics, and the abdominal lymphatic channels have also been so demonstrated. As stated above, it is surprising how small quantities of opaque medium, such as 1–1.5 ml., give good delineation of the lymph vessels when there is little sign of dilatation. If, however, gross dilatation and varicosity exist, a much larger quantity may be necessary to demonstrate all the ramifications of these vessels and to outline the more proximal lymph vessels in leg and arm. With care and co-operation much interesting information concerning the state of the lymphatic system can be gleaned by this type of examination.

FIG. 4.—Idiopathic lymphoedema. Lymphangiogram shown in Fig. 3. Operation gave considerable amelioration.

For the limbs our technique has been as follows. Non-screen film: 65 kV, 65 mA; time, 2 seconds; distance, 48 in. (122 cm.).

For the thicker parts:—cassette and grid: 80 kV, 45–50 mA; time, 1.5 seconds; distance, 48 in. (122 cm.).

It is important that each new technique should be thoroughly supervised by a radiologist, as difficulties occur in operating theatres which may require special equipment, and discussion between surgeon and radiologist may be necessary to reconcile the problems with which each is faced, in order to evolve a satisfactory solution to the problem and obtain the best possible results.

Results

The method has been used to study lymph vessels in lymphoedema praecox, post-mastectomy oedema of the arm, post-phlebitic ulceration and oedema of the leg, congenital arteriovenous fistulae, and other diseases. Some of the findings have been reported elsewhere, and it is not proposed to give further details here, but instead to describe some examples illustrating the technique.

A normal lymphangiogram is shown in Fig. 2. The lymph trunks remain the same width in their course up the limb, unlike veins which become wider. Bifurcation occurs frequently, so that the trunks appear to multiply as they pass upwards. The ampullae of valves are often seen.

The lymphangiogram shown in Fig. 3 was taken from the leg of a patient with idiopathic lymphoedema (Fig. 4). The lymph vessels are tortuous and wide. There is both

lateral and retrograde flow of the dye into other lymph vessels. These features are never seen in normal lymphatics.

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THE DELLWOOD FIRE

BY

MARIAN E. COX, L.R.C.P.&S.I., D.C.H.
Registrar, Paediatric Department, Royal Berkshire Hospital, Reading

BARBARA F. HESLOP, M.D.
Research Fellow, Department of Morbid Anatomy, Hospital for Sick Children, Great Ormond Street, London

J. J. KEMPTON, M.D., M.R.C.P.
Paediatrician, Reading Area Hospitals

AND

R. A. RATCLIFF, M.D.
Assistant Paediatrician, Reading Area Hospitals

In the early morning of Easter Sunday, April 18, 1954, a fire occurred in the nursery of Dellwood Maternity Home, Reading, which resulted in the death of 13 newborn babies. Dellwood is a general-practitioner obstetric unit of 17 lying-in beds dealing with normal cases. The hospital staff serve in a consultant capacity. The building is about fifty years old and there have been a few structural alterations during the twenty-four years of its use as a maternity home. The nursery measures 20 by 12 ft. (6.1 by 3.6 metres), with two doors and two windows: the floor boards are of deal covered by linoleum.

The fire was caused by the flue of a hot-water boiler which in September, 1953, had been moved so that it ran beneath the floor of the nursery. It has been established by subsequent inquiry that the installation of the flue complied with the local building regulations, though the experts who assisted the Regional Board in their inquiry agreed that the regulations need overhauling. It seems likely that the fire began slowly, with much smouldering of wood over a large area of floor. This, the destructive distillation of soft wood and also of some linoleum, filled the room with thick smoke, until finally part of the floor caught alight and the flames spread to one of the cots. It is thought that the room may have been filled with smoke for between 20 and 30 minutes.

There were 15 babies in the nursery, the doors of which were closed, while the windows were kept slightly open. A gas fire was burning. A nursing staff of two were on duty and the nursery was visited at intervals during the night, the last visit before the fire being about 3.15 a.m. The fire was discovered by one of the sisters*.

*Sister E. M. Holland was later decorated with the George Medal by Her Majesty the Queen.

at 4 a.m., and she immediately began to remove the babies from the room while help was being called. While removing the first babies she received considerable burns of face and arms and was in great distress from inhalation of smoke; she continued to bring them out one by one, and finally collapsed when the last one had been carried out. She was subsequently admitted to hospital.

One of us (R. A. R.) first saw the babies at 4.30 a.m. One whose cot had caught fire was dead following extensive burns involving the whole body, with some charring. Three others were transferred to the Battle Hospital at once and placed in oxygen boxes. One of these had some superficial burns of the face. All three were limp and pallid and in great respiratory distress. There was much clear viscid discharge from nose and eyes and complete nasal obstruction. The remaining 11 babies were in good general condition, but all were coughing a little and had some discharge from the nose and eyes. Their colour was generally good apart from slight occasional cyanosis produced by coughing attacks and interference with breathing by nasal obstruction. During the day there was some deterioration. Respiratory rates were rising, and in all cases cough had increased: a little clear yellow fluid was occasionally coughed up or aspirated. Scattered rales, in every case, became audible in the afternoon and evening. Oxygen boxes had by this time been obtained for all the cases.

That evening it was decided to clear a hospital ward and make special arrangements for nursing staff, and early on Monday morning all the surviving babies were transferred in oxygen boxes to the Royal Berkshire Hospital. An alarming increase in respiratory obstruction developed in all the cases, and on Monday evening it seemed unlikely that any of the babies would survive. The appearances were similar to those with which we are familiar in asphyxia due to hyaline membrane, with, in addition, signs of upper respiratory tract irritation; but these were strong infants several days old, and were making very forcible efforts to breathe, whereas in hyaline membrane asphyxia we are dealing usually with a shocked or feeble baby. Thus the characteristic contrast between struggling respiratory effort and poor breath sounds on auscultation was very striking.

Two of the babies began to improve after the third day and finally appear to have made a good recovery. There is no reason to suppose that these two suffered less exposure to the smoke than any of the others.

Treatment

All the babies were given oxygen, the first three being placed in oxygen boxes on admission to hospital, and the remainder (who at first stayed at Dellwood) being similarly treated later on the first day when chest signs were appearing and extra boxes had been obtained. Before this, some oxygen was given by tube and funnel or catheter when coughing attacks led to cyanosis. Mucous secretions were aspirated at intervals as needed, and 5% sulphacetamide was applied to the nose and eyes. Penicillin was given in all cases, starting on the morning of the first day with 100,000 units eight-hourly by injection. The dose was later reduced and given orally to the babies who survived. Humidification was maintained by electric steam-kettles.

At midday on Monday, the day after the fire, streptomycin (100 mg. eight-hourly) and cortisone (50 mg., then 25 mg. eight-hourly) were added to the treatment.

The babies were nursed with the foot of the cot raised and were kept for most of the time in a high concentration

of oxygen, with a flow of four to five litres a minute. The position was altered from side to side at two-hourly intervals, and aspiration of the nose and pharynx was carried out by catheter and electric sucker very frequently. Temperature and respiratory rates were recorded at hourly, and later at two-hourly, intervals. Feeds, at first of glucose–saline and later of milk mixture, were given by oesophageal tube during the first 48 hours. Aspiration of the trachea was attempted in three cases without apparent benefit, and hardly any mucus was obtained by this method. Gastric oxygen was given to several babies *in extremis*, and in one of these it was noted that the colour improved and was maintained for about half an hour after all respiratory movement had ceased.

In those babies who survived the first 48 hours percussion drainage was attempted in addition to postural drainage and frequent changing of position. This seemed to produce some good results: mucus was coughed up and aeration seemed to have improved. In one baby (one of those who recovered) a large bronchial cast was aspirated from the nose on the sixth day, after one of these periods of percussion drainage.

Outline Course of Individual Cases

Case 1.—Male aged 6 hours. Died during fire. Extensive burns and charring.

Case 2.—Female aged 6 days. Superficial burns of face and chest and oedema of eyelids. Respiratory distress was apparent immediately, with severe coughing, grey cyanosis, and much mucous discharge from nose and eyes. Was transferred to Battle Hospital and placed in oxygen and steam, with frequent local treatment to nose and eyes. Penicillin powder applied to burns. Progressive deterioration throughout the day until death at 10.33 p.m. Survived 18½ hours.

Case 3.—Male aged 9 days. Very slight scorching of face. Respiratory distress and cyanosis from onset. Transferred to Battle Hospital and placed in oxygen box. Much greenish-yellow mucus was aspirated from nose and pharynx. Slight deterioration throughout day. Feeds of glucose–saline given by tube were retained. At midday trachea was aspirated but no mucus obtained. Condition became steadily worse during the night. Died at 4.55 a.m. on the second day. Survived 25 hours.

Case 4.—Female aged 2 days. Had seemed to be in good condition at first and during the first day. Onset of dyspnoea and cyanosis during early morning of Monday, with subsequent rapid deterioration. Died at 6.30 a.m. on the second day. Survived 26½ hours.

Case 5.—Female aged 4 days. Some cyanotic attacks with coughing on first day, but general condition was fairly good and feeds were retained well. Slowly increasing distress on second day as the respiratory rate rose. Died at 10.45 a.m. on the second day. Survived 31 hours.

Case 6.—Female aged 8 days. Condition seemed fairly good at first, but the respiratory rate rose to 60 during the first 24 hours, after which dyspnoea increased progressively. On account of the very great respiratory distress the trachea was aspirated on the second day on two occasions, but this produced no relief and very little mucus was obtained. Died at 6.10 p.m. on the second day. Survived 38 hours.

Case 7.—Male aged 3 days. Well, apart from slight cough during the first 12 hours. After this period similar course to Case 6. Strong baby, making violent respiratory efforts. Period of intermittent breathing preceded death at 6.30 p.m. on the second day. Survived 38½ hours.

Case 8.—Male aged 4 days. After some slight intermittent dyspnoea and cyanosis during the first 24 hours appeared to be improving. Much stained mucus had been aspirated from the pharynx. There was a rapid deterioration with increasing dyspnoea during the evening, and he died at 9.10 p.m. on the second day. Survived 41 hours.

Case 9.—Male aged 3 days. In good condition in early stages, symptoms gradually increasing after the first 24 hours. Died at 10 p.m. on the second day. Survived 42 hours.

Case 10.—Male aged 7 days. This baby showed early signs and was one of the three (with Cases 2 and 3) who were transferred to the Battle Hospital immediately after the fire. He had improved, respiratory rate had fallen, and feeds were retained satisfactorily. Cyanotic attacks and rising respiratory rate recurred during the night of Monday and became more severe in the early morning. One unsuccessful attempt was made to suck out the trachea. A period of several hours of marked head retraction preceded death at 4 a.m. on the third day. Survived 48 hours.

Case 11.—Female aged 6 days. This baby remained in fairly good general condition until 24 hours after the fire, respiratory rate remaining in the region of 40 a minute. There was very slight scorching of the face and one hand. Pyrexia with temperature 102° F. (38.9° C.) developed during the second night, and, following this, chest symptoms and signs increased until she died at 10.24 a.m. on the third day. Survived 54 hours.

Case 12.—Male aged 2 days. Gradual development of symptoms during the first 24 hours, after which there seemed to be a steady improvement. At 2 a.m. on Tuesday became hyperpyrexial; temperature 107° F. (41.7° C.). This subsided, but the baby did not improve further, and after repeated attacks of cyanosis and development of head retraction, died at 11 a.m. on the third day. Survived 55 hours.

Case 13.—Female aged 3 days. Course was very similar to the previous one, with pyrexia—temperature 104° F. (40° C.)—during the second night and final deterioration after early improvement. She died at 12.50 p.m. on the third day. Survived 57 hours.

Case 14.—Female aged 3 days. The early course was similar to previous cases, but there was some improvement in aeration during the third day and subsequently as mucus was coughed up and aspirated. Percussion drainage seemed to be increasingly effective, and on one occasion was followed by the production of a large cast. From the fifth day there was a steady improvement, though an *x*-ray film (Fig. 1) on the sixth day showed that extensive areas of collapse were present. Cortisone was reduced to 12.5 mg. eight-hourly on the fourth day, and stopped after a further 24 hours. Oxygen was gradually withdrawn and penicillin and streptomycin were stopped on the ninth day. On the eleventh day an *x*-ray film

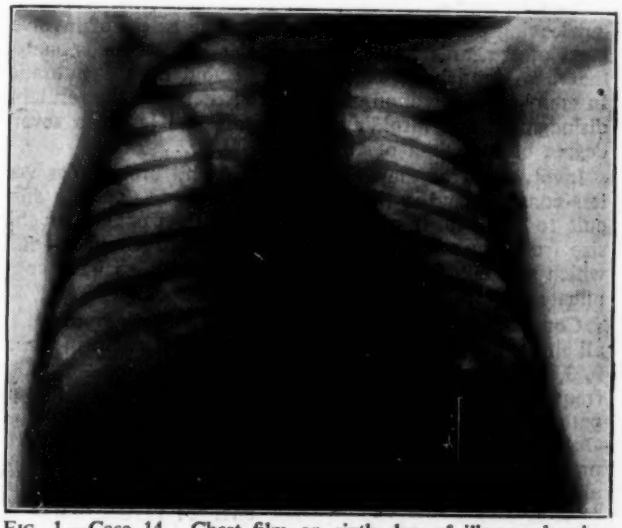

FIG. 1.—Case 14. Chest film on sixth day of illness, showing extensive areas of collapse consolidation. Later films show complete clearing.

showed considerable clearing. There were several alarming cyanotic attacks at this late stage, but these were of brief duration. Breast-feeding was re-established, and she was discharged home fully breast-fed and symptom-free on May 5, 17 days after the fire. Subsequent *x*-ray films show clear lung fields.

Case 15.—Male aged 7 days. Course was parallel to that of Case 14, and this infant was fully breast-fed by his mother when he was discharged on May 5. Both mothers had been admitted to re-establish feeding as soon as the babies began to improve. As in Case 14, there were several brief but alarming cyanotic attacks during convalescence associated, it seemed, with the separation of bronchial casts. Some yellow staining of the skin in both these babies persisted until a few days before their discharge.

Pathology

Post-mortem examination of the respiratory tract was carried out initially by Dr. J. A. Hardy, police surgeon at Reading. Permission was given by the coroner for further investigation of the specimens to be undertaken, and accordingly one lung from each case excepting the first was made available for examination in the Department of Morbid Anatomy, Hospital for Sick Children, Great Ormond Street.

Naked-eye Appearances

The most striking changes were seen in the bronchial tree, where the formation of a membranous cast had occurred in each case. In Cases 2 and 3 this was still firmly attached to the bronchial wall, and consisted of a thick layer of greenish-yellow material flecked with carbon. This replaced the normal shiny bronchial mucosa. A little yellow watery fluid was also present in the bronchial lumen. In those cases which survived longer, separation of this membrane from the bronchial wall had occurred. The cast now appeared as a firm tubular structure surrounded or indented by a quantity of sticky brownish mucoid material. Separation occurred initially in a patchy fashion so that only in those cases surviving longest was it possible to extract a whole cast of the bronchial tree without leaving portions behind (Fig. 2). The extent of involvement of the large bronchi was similar in all cases, none of the main branches being entirely devoid of a membrane. In many cases secretion of mucus together with the resultant dislodgment and infolding of the cast had led to a severe degree of bronchial obstruction.

FIG. 2.—Cast of bronchial tree removed at necropsy. Black flecks of carbon are seen scattered throughout the specimen.

Involvement of the smaller bronchi and bronchioles was less constant, and in the gross specimen it was usually difficult to distinguish cast formation in air passages of this size from the bronchiolitis and adjacent bronchopneumonia which was subsequently shown histologically to have complicated several cases.

Congestion and oedema of the lung tissue was present in all the specimens, but was particularly noticeable in Cases 2, 3, and 4. Interstitial emphysema and oedema were also frequently seen, with resultant accentuation of the mosaic pattern produced on the pleural surface by the lobules. Occasional large interstitial emphysematous bullae were also present. There were considerable areas of collapse and alveolar emphysema in all specimens, although the quantity of lung tissue involved in these changes varied somewhat from case to case. In most of the lungs collapse predominated over emphysema. All the specimens showed pleural haemorrhage, varying in size from scarcely perceptible petechiae up to extensive haemorrhagic areas involving a considerable proportion of the pleural surface.

Histology

Examination of the larger bronchi showed that, while the greater part of the epithelium had been destroyed, not all areas were quite so severely affected, and in a few places the epithelium had been spared completely. This was particularly noticeable where relative protection had been afforded by mucosal folds, or near the ducts of mucous glands. In the less severely affected regions the epithelial cells had desquamated either singly or in clumps. The cytoplasm was swollen, homogeneous, and intensely eosinophilic, and the nuclei either showed degenerative changes or had disappeared. In the more severely affected parts individual cellular detail was less evident. The necrotic cells had fused together, replacing the epithelium by a densely eosinophilic membrane containing occasional nuclear remnants and patchy aggregations of carbon particles.

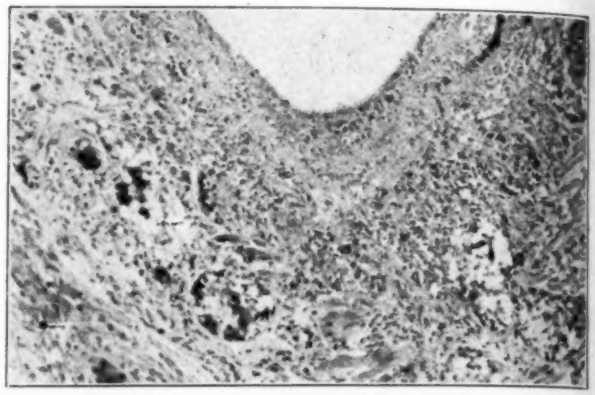

FIG. 3.—Destruction of bronchial epithelium with formation of a thick membranous cast. Cast contains carbon particles and is still attached to the bronchial wall. (×90.)

The bronchial walls were intensely congested and oedematous, and frequently haemorrhagic. Moderately numerous inflammatory cells were present in the cast and adjacent bronchial wall. These consisted of approximately equal numbers of polymorphs and mononuclear cells. At a later stage secretion of mucus from the underlying glands occurred, with resultant separation of the membrane from the bronchial wall. This process was barely starting in Cases 2 and 3, in which most of the cast was still attached (Fig. 3), but became progressively more advanced in those cases surviving longer, when large quantities of mucus could be seen lying between the cast and the bronchial wall. In some of the bronchi this led to complete occlusion of the lumen. Where separation had occurred the bronchi were sometimes devoid of a lining epithelium, although usually a few of the basal cells had been spared. No definite evidence of epithelial regeneration was seen in any of the specimens.

Cast formation in the bronchioles was very much less extensive, the majority being uninvolved in this process. In several cases there was acute bronchiolitis, which in Cases 2, 3, and 4 had progressed to well-developed bronchopneumonia. Cases 8, 10, and 11 showed very much earlier bronchopneumonic changes. This bronchiolitis was independent of the presence of bronchiolar casts, and was commonly seen where the latter was absent. The inflammatory exudate in the bronchiolar walls was very much more cellular than that seen in relation to the casts in the large bronchi.

The alveoli were congested and oedematous, and showed well-marked collapse and emphysema. In addition to the oedema fluid the alveoli contained carbon particles, small quantities of eosinophilic fibrillary material which gave negative stains for fibrin, and moderate numbers of mono-

nuclear cells, many of which were vacuolated. Occasional squames were present in some of the lungs, but no hyaline membrane was seen. The interstitial tissue was oedematous and often contained large air spaces (Fig. 4). There were numerous interstitial and intra-alveolar haemorrhages. The latter were not particularly extensive except in Case 5, in which large areas of the lung were involved, giving an appearance reminiscent of pulmonary infarction.

FIG. 4.—Interstitial emphysema, with large air spaces in interlobular septum. (×55.)

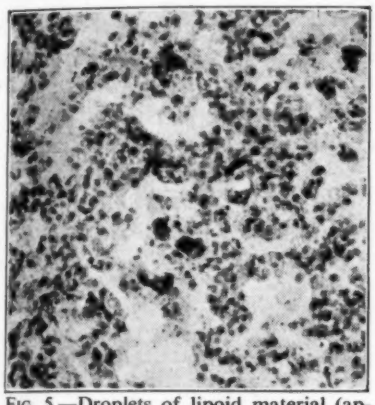

FIG. 5.—Droplets of lipoid material (appearing black) within the alveoli. (×200.)

Frozen sections showed the presence of lipoid material in the alveolar macrophages, and also considerable deposits of similar material extracellularly in the alveoli (Fig. 5). To a less extent lipoid was also present in the bronchial casts and in some of the bronchopneumonic foci. As the most extensive deposits occurred in areas where there was no acute inflammatory reaction, it was assumed that the material was not severely irritant and could not be held responsible for the bronchial lesion. It was present to a greater or less extent in all the lungs, and its distribution, together with the quantity present, suggested that its origin was exogenous rather than endogenous. In order to ascertain whether the lipoid could have been a constituent of the smoke, small portions of painted wood and linoleum were distilled separately. In each case a brown oily distillate was obtained. No attempt was made to analyse this, but it was smeared on slides and subjected to the same staining procedure (Scharlach R) as the histological material. In the case of the distillate from the painted wood, small quantities of positively staining material were obtained, while in the case of the linoleum a considerable proportion of the distillate stained positively by this method. Thus it seemed reasonable to infer that the lipoid material in the lungs had been inhaled in the smoke.

From the gross and microscopical appearances it was not possible to determine which cases had suffered the greatest exposure to the smoke, nor was it possible to correlate the severity of the bronchial lesion with the quantity of either carbon or lipoid present.

Discussion

These 12 babies died as a result of progressive bronchial occlusion together with pulmonary oedema and infection. The first three babies to die showed less severe obstruction than the subsequent cases; little separation of the cast had occurred, but pulmonary oedema was much more pronounced, and there was extensive bronchopneumonia. In the later cases pulmonary oedema and infection were less prominent features, but bronchial obstruction had become much more complete as a result of secretion of mucus and displacement of the membranes cast into the centre of the bronchial lumen.

The retention of such large quantities of mucus within the bronchial tree was due largely to two factors. Firstly, much of the mucus was trapped between the bronchial wall and the cast, and removal was often further impeded by the fact that adjacent parts of the cast were still adherent to the bronchial wall. Secondly, the removal of mucus was prevented by the destruction of most of the ciliated epithelium.

The formation of the bronchial cast was attributed to irritant substances present in the smoke to which the babies were exposed. Membranous bronchitis is a recognized, though fortunately uncommon, complication of some infections, notably diphtheria, and has also been reported following the inhalation of certain war gases (Winternitz, 1920), nitrous fumes (von Oettingen, 1941), and after exposure to atomic radiation (Liebow *et al.*, 1949). Lesions very similar to those described above were reported as occurring in some of the victims of the Coconut Grove fire.

There is every reason to believe that if the babies had survived the initial hazards of pulmonary oedema and infection, and the later period of bronchial obstruction, complete restoration of the bronchial epithelium might have occurred, regeneration proceeding from the surviving islands of epithelium in the mucosal folds and duct orifices (Wright, 1950).

If the course of events is reviewed in the light of subsequent investigations the most important question that arises is whether anything further could have been done to help these babies. Atropine might have been given in sufficient doses to diminish secretion. It might, however, also have made secretions more viscid and less likely to separate. Humidification by mist, perhaps with the addition of a detergent, might have been used, but this could have led to fatal increase in the already great amount of fluid in the lungs. Cortisone might perhaps have been given earlier and in larger doses; but in addition to diminishing exudative responses cortisone has other effects, including that of promoting fluid retention and possibly diminishing resistance to infection. More vigorous and intensive aspiration of the lower respiratory tract might have been attempted, including perhaps aspiration through tracheotomies, but such procedures in the newborn have their own risks and probably a high mortality. They might, however, have been effective in the babies who survived to the third day, when some of the casts were beginning to separate.

The simple measures which were attempted were carried out by ourselves and by the nursing staff. The latter, working in eight-hour shifts, showed skill and gentleness that were all that could be desired. Percussion drainage was at first performed by one of us, but later, too, this was taken on by the nursing staff in some cases.

A tragic event such as this should not perhaps be used as an argument for or against any system of care. The custom of putting all the babies into a nursery for the night so that the mothers can sleep undisturbed is a widespread one, and is particularly the rule in smaller maternity homes. Quite apart from the possibility of a disaster such as this, the system is, we think, a bad one, and we would repeat the opinion frequently given by paediatricians and obstetricians that the proper place for the normal newborn baby is in a cot close to the mother's bed.

Summary

An account is given of the Dellwood fire which caused the death of 13 newborn babies. Two babies survived and are now apparently normal. One baby was found dead. The others died within three days of the fire.

The symptoms were those of increasing respiratory distress, pyrexia, cough, and cyanotic attacks. Death was due to bronchopneumonia in the first 24 hours, or later to bronchial obstruction caused by casts consisting mainly of fused necrotic epithelial cells. The bronchial changes were due to inhalation of smoke.

Treatment included oxygen, chemotherapy, cortisone, percussion and postural drainage, and aspiration of mucus from the mouth and nasopharynx. Tracheal aspiration and gastric oxygen were used, but the results were disappointing. The question of possible alternative treatment is discussed.

Among the many who helped us during these babies' illness we would like especially to record our thanks to Dr. B. Schlesinger, Dr. D. Foskett, and Mr. E. Hunt Williams. Acknowledgments are due to Dr. J. A. Hardy, the police surgeon in Reading, who on H.M. Coroner's instructions carried out the post-mortem examinations. In later investigations valuable technical advice was received from Mr. L. C. Nickolls, Director of the Metropolitan Police Laboratory. Valuable help was received in the laboratory investigations from Dr. C. de Courcy and Mrs. A. Hopkins. We are also grateful to Dr. M. Bodian for assistance in the preparation of this paper, and to Mr. Derek Martin, of the Department of Medical Illustration, Great Ormond Street, for the photographs.

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THE SOCIAL AND PSYCHOLOGICAL BACKGROUNDS OF TUBERCULOUS CHILDREN

BY

DINA ROSENBLUTH, B.A.

AND

JOHN BOWLBY, M.A., M.D.
Deputy Director, Tavistock Clinic

One of the projects undertaken by a research team investigating the effects on personality development of separation from the mother in early childhood was a follow-up of children who, because they had tuberculosis, had been separated from their mothers, and in a sanatorium, for a period during their first years of life (Bowlby, Ainsworth, Boston, and Rosenbluth, 1955). This required us to investigate the social background of these children, and the present study is a by-product of the main research. It gives some findings relating to the economic and housing conditions, the extent of family illness and disruption, and some of the psychological attitudes found among members of these families during the year 1950. Although we are aware that what is described will not be new to workers in the field of tuberculosis, our impression is that that knowledge exists in rather a fragmentary form.

The gross sample studied was obtained by extracting from the records of a sanatorium the record of every child admitted between birth and 4 years, between January 1, 1940, and November 30, 1948, inclusive. From this sample were eliminated children whose primary tuberculosis was complicated by bone or abdominal infection, those who had left the county of Middlesex, who had gone into the care of other institutions, or who had died, and those who were not yet of school age. The resulting sample consisted of 60 children—41 boys and 19 girls. They had all returned to their homes and were attending schools in the county. The present addresses of the children were traced with the help of the chest clinic and education authority records.

The need to make direct systematic inquiry of the families in which we were interested was recognized by the staffs of chest clinics, and in arranging the interviews it was of great help to be able to state that both the sanatorium and the local chest clinics were co-operating in the research. The warm welcome and readiness to talk which the psychiatric social worker met with in most families are believed to be a tribute to the sanatorium, which most families remembered with gratitude. Lack of co-operation was on each occasion related to reluctance to disclose an especially difficult or disturbed family situation.

The total sample of 60 children came from 57 families. Two families, containing three children, refused altogether to co-operate, and one of two siblings was in a residential school. The total number of families remaining is therefore 55, containing 56 children.

The average length of interviewing time was four to five hours, usually spread over two or three visits. The psychiatric social worker spent a little time at the beginning of the first interview explaining the purpose of the research. Once the family had agreed to co-operate she attempted to guide the interview so as to cover the main points on which information was sought. Where there was reluctance to give information this was not pressed for. On the other hand, the parents often talked at length about their problems, and in many cases revealed their attitudes to tuberculosis and to the tuberculosis service. It was thus, incidentally and unasked for, that much of our material was obtained.

Economic and Housing Conditions

The families were rated for economic and for housing conditions, each on a four-point scale. The rating "A" for economic conditions implies an income on which the family could manage fairly well and afford an annual holiday. The rating "B" implies an economic situation that is fairly adequate. The rating "C" implies a rather poor income, usually only one parent being at work, in an unskilled occupation, and the family finding it difficult to make ends meet; a summer holiday was out of the question, or possible only once in a while and at great sacrifice. The rating "D" implies that the families suffered real economic hardship. These were the families the mothers of which were widows and had to live on widows' pensions supplemented by a little earning of their own or by the National Assistance Board. The distribution of ratings is shown in Table I.

TABLE I.—*Economic Circumstances of 55 Families*

Rating	No. of Families
A: Comfortable	6
B: Fairly adequate	20
C: Poor	16
D: Economic hardship	13

Not infrequently the psychiatric social worker heard accounts of severe economic hardship in the parent's own childhood, and also during the pre-war or early war years, when the sample child was an infant. But with the great majority of the families the economic situation had taken a marked turn for the better in the post-war years. At the time of the inquiry the black spot was the 13 families rated "D"

which constitute one-quarter of the families concerned, and which were living on a bare subsistence level. Twelve of these families were existing on widows' pensions, and in the other the father had been ill for the past two years and the family lived on National Assistance money. It seemed that they could not afford all the food they should have, and the psychiatric social worker heard stories of children having to stay away from school on rainy days because they did not possess adequate clothing.

Most of the families lived in good, usually small, semi-detached suburban houses, often on council estates. The rating "A" for housing conditions indicates that the house was very good and there were sufficient rooms for the children to have their own bedrooms; rating "B" also implies good housing, but with the need for some sharing of bedrooms; rating "C" was given either where the house was in a poor condition or where, although the house was a reasonably good one, it was not large enough for the family; rating "D" implied that the house was in a poor condition and there was inadequate space. The distribution of ratings is shown in Table II.

TABLE II.—*Ratings of Housing Committee*

Rating	No. of Families
A: Very good	10
B: Good	24
C: Poor	15
D: Inadequate	6
	55

Of the six families living in inadequate housing conditions, one lived in a condemned house, three had only part of a house each with quite insufficient room for the family, and the two others lived in old-fashioned small houses where there was gross overcrowding.

Family Illness and Disruption

The extent to which there had been illness in the family with consequent disruption was very great. In the 55 families, only the children of 29 were living with both their parents in an intact family. The remaining 26 families (containing 27 children) were all disrupted, either through the death of one or other of the parents (in 22 families) or because the parents were separated (in 4 families).

In the great majority of cases this disruption was due to tuberculosis, either in the past or in the present. Nineteen parents and 8 siblings had died from the disease. Altogether infection or death from the illness had occurred in a parent or sibling in 33 of the families, leaving only 22 families in which the child studied was the only case. Table III presents the incidence of cases of tuberculosis in the families

TABLE III.—*Extent of Tuberculous Illness in the 55 Families*

	Both Parents	Father Only	Mother Only	One Sibling	More than one Sibling
Past tuberculosis	1	16	11	11	5
Death from tuberculosis	1	16	1	6	1
Present tuberculosis	—	—	9	2	—

other than the sample child. In addition to the deaths shown in this table, two fathers and three mothers had died of other causes.

Table IV shows the presumed source of the child's infection. It will be seen that about half the children were believed to have been infected by one of their parents.

TABLE IV.—*Contact Through Whom Child was Thought to Have Been Infected*

Contact	No. of Children
Father	18
Mother	11
Grandparents, uncle, or aunt	10
Neighbour	4
Contact unknown	13
	56

In addition to the 22 families which had been disrupted by death, four were not intact for reasons of illegitimacy (1), divorce (2), and separation (1).

Even among the 29 children who were living with both parents family life was not always normal. In two cases the parents had, since the child's birth, separated for a while, but had later decided to live together again. In one of these the ostensible cause for the separation had been father's dread of mother's tuberculous illness. There were four families in which the mother was ill with tuberculosis at the time of inquiry, and in several other cases the mothers were very preoccupied with their own health and worried in case they had tuberculosis. In two more families the fathers were ill, but the nature of the illness was not known to the psychiatric social worker. In a further eight families father, mother, or a sibling had had tuberculosis at one time or another, and family life had therefore been upset owing to the absence of a member in a sanatorium, with consequent anxiety about the health of other members of the family. This leaves a balance of only 13 families whose family life had been relatively undisturbed.

Attitudes and Feelings

In the course of the inquiry it became apparent what far-reaching and complex psychological repercussions were aroused by the existence of a tuberculous illness in a member of a family. Many parents spent a considerable time in discussing with us their fears for their own or their children's future health, or whether or not to tell the child about his having had tuberculosis in early childhood. As a result, much incidental light was thrown on the attitudes to the illness and on the ways these had influenced their relationship to their children and their neighbours. As these attitudes to tuberculosis were not the focus of interest, they were not systematically investigated and therefore there are gaps in our information. In the description which follows it is thus not possible to give accurate figures of the numbers of families concerned.

Fear of Tuberculosis

As was only to be expected in view of the extent of the illness and the number of deaths among these families, a conscious fear of it and its implications was very widespread. In a surprising number of cases (about one-fifth), however, the parents dealt with these anxieties by attempting to deny that there had been any tuberculous illness at all. The most striking was where a father, whose wife and son had both been in the sanatorium for considerable lengths of time, attempted to convince the psychiatric social worker that he had *x*-ray plates to prove that neither of them had had tuberculosis at all. He felt that there had been some plot to take his family away from him. (His wife had been infected by her mother, whom she had nursed until the mother had died of tuberculosis.) This man does not approve of his son going to the chest clinic now. He was clearly very paranoid, extremely suspicious, and willing to co-operate in the research only after the psychiatric social worker had explained that we were not really concerned with the reasons for the child's having had to go to hospital but only with his subsequent development.

Although this man's reactions were exceptional, similar attitudes in lesser degrees were present in quite a number of parents. There were cases where a mother or father had in the past refused to go to a doctor or into a sanatorium after the diagnosis had been made, staunchly denying that there was anything wrong with them. Some of them had died at home, and before doing so had infected their young child. One woman told the psychiatric social worker that it was almost a relief to her when her husband died, as she felt that that had saved the child's life, because he had refused to let the child be seen by a doctor. The father of one family and the mother in another were ill at home at the time of the investigation, afraid that they might

have tuberculosis, but protesting that there was nothing really wrong and that they did not think it was necessary to consult a doctor.

Several parents maintained that they did not know why their children had had to go to the sanatorium. Even where the hospital stay had been a very long one they insisted that it had probably been only for observation, not because the child had really been ill. This attempt to deny the illness was clearly bound up with a tremendous fear of it; in some cases both attitudes existed quite consciously side by side. One mother, who had herself on two occasions been in a sanatorium, and whose child had had tuberculosis too, was in a continuing and constant panic about this illness. She remarked several times during the interview, however, that she did not think that either she or her child had really been ill, and clung to the belief that no doctor had ever told her in so many words that either of them had actually had tuberculosis. At another time she said, however, that she did not suppose they would have been kept in hospital so long if they had not been ill.

The attempt to deny the illness because of so overwhelming a fear of it thus led, in a number of families, to a failure to take proper measures for prevention and treatment. These findings are consistent with those of Gore and Hartston (1953), who, reporting on the results of questioning more than a thousand mothers of young children, found that 69% of them thought that there are many people who are afraid to be examined in case they have tuberculosis.

In a number of families (again about one-fifth) the reaction was the opposite to denial, and took the form of constant hypochondriacal fears for the families' health even in the face of frequent reassurance by their doctors that there was now nothing wrong; their lives appeared to be permanently overshadowed by fears for the children's health. Some mothers were so worried about their own health that it was difficult to get them to talk about anything else. One woman in particular described in detail all the symptoms from which she was suffering, which were identical to the symptoms which her own mother had had just before she had died of tuberculosis. Her doctor had assured her that there was in fact nothing wrong with her, but she was still very afraid that she was ill, and was also constantly watching her children's health for the slightest signs of indisposition. She said that she would be reassured only if she had an *x*-ray examination, but that her doctor would not give her a letter for an examination at the chest clinic, and without it the chest clinic would not see her.

In some cases the children had caught their parents' fears. One 13-year-old girl was said to be constantly preoccupied with her health and was always weighing herself. This girl was afraid to go to bed at night and always found one excuse after another to put it off for as long as she could. Frequently, when her mother finally said she must be tired now, she would reply, "Who wants to go to bed? People die in bed." She was said to grind her teeth, to sleep-walk, and often to talk and shout out in her sleep. Another young girl was described as a "proper old woman" by her mother, always fussing about her health and demanding aspirins.

Parents' Feeling of Guilt

Even where there were no great fears for their own or their children's health a certain pampering and overprotectiveness towards the child who had been ill was fairly general. Although this attitude is a very natural and understandable one after the child's return from the sanatorium, it frequently continued and was still very pronounced at the time of the investigation, years after the child's complete restoration to health. In these cases it seemed connected with the mother's feeling of guilt and assumption of personal responsibility that the child should have been ill at all. In some few cases there might have been legitimate grounds for the mother's feelings that had she taken greater precautions the child might not have been infected. One woman, for instance, said that she was entirely to blame for the child's illness because, when he was a toddler and his father was ill at home, she was on one occasion not quick enough in removing the father's eating utensils and found the child with the father's spoon in his mouth.

Even where there was no reason whatsoever to think that the parents were in fact responsible for the child's illness through any lack of precaution—for instance, where the contact through whom the child was infected was unknown—some mothers said that they somehow felt guilty that their child should have been ill. In other cases it appeared to the psychiatric social worker that the parents protested too much that the blame for the illness lay elsewhere (with the grandparents, neighbours, etc.), and it seemed that unconsciously they also felt it was their own fault.

This widespread feeling of guilt no doubt played its part in leading a majority of the mothers to an initial overanxiety and overprotection of the child. However, such attitudes are almost inevitable in a mother after her child has been away from her for a long time and especially if he shows some of the emotional disturbances which commonly follow such separations. In consequence, in considering the subsequent relations of mother and child, it is not easy to determine how much is due to the mother's sense of guilt and how much to the child's disturbance following separation and to the mother's attempts to meet the disturbance.

Attitude of Overprotection

It seemed that some of the mothers soon realized that it was important that their child should be treated the same as his siblings and so should not feel that he was a special case. Other mothers said that only after a while did they realize, through bitter experience, that the child was harmed by this attitude of overprotection, of constant watchfulness and anxiety about his health. In these cases the children had reacted by considering themselves special cases, or else had rebelled and become difficult to manage. Some of these mothers were able gradually to relax and allow their children more independence, but in some cases difficulties persisted; the children continued to insist that they must have special treatment because they had been ill. Other parents were quite unable to overcome their constant overanxiety, and seemed to be unaware that they might be harming the child by it.

Although the knowledge that tuberculosis is an infectious illness was general among the 55 families, there quite often persisted side by side with it the belief that it is a hereditary disease. In several families there was some discussion and a wish for reassurance that the children, who are at present all well and not in contact with any tuberculous person, would grow up healthy; in particular, anxiety was expressed that, because there had been tuberculosis in the father or mother's family, the children were likely later to fall ill too. No doubt because of the great frequency of cross-infection in families the belief that tuberculosis is hereditary dies hard. Gore and Hartston (1953) found it expressed by 43% of the mothers questioned.

Should Parents Tell?

At the same time, much more surprisingly, it seemed to be taken almost for granted among many families that psychological factors influence both the incidence and the course of the illness. In those cases where the parents raised the problem whether or not to tell their children that they had been ill in early childhood, one of the main arguments against it was that the child might later worry and thus again develop tuberculosis. One woman said of her husband that when he fell ill she felt that he did not stand much chance of recovery as he was such a worrier. Another family agreed to co-operate in the research only when they were reassured that the child would not, through the psychiatric worker, get to know that he had ever been

in a sanatorium; they were determined never to tell him, as if he were to know about it he would worry and therefore fall ill again. Another woman said that her sister had announced that, should she ever have tuberculosis, she would not be ill long; when subsequently she did fall ill she died within a few months. This same woman was also determined never to tell her daughter that she had been ill, again for fear that the girl might worry and thus inevitably fall ill again. Many similar remarks showed that there was a very general belief that there is a close interaction between psychological attitudes and the course of the illness.

These attempts to keep the illness a secret from the child were perhaps also another indication of the mother's unconscious feeling of guilt that the child should have been ill at all and of the fear that he would blame her for it. Another important factor, however, was that it was felt that having had tuberculosis was equivalent to "being branded for life," a phrase the psychiatric social worker heard several times. It was felt to imply both a social and a vocational stigma. There were fears whether the child later might have difficulties in finding employment if he knew, and therefore would have to tell, that he had once had tuberculosis. An adoptive mother of one of the children said that she had not disclosed the fact that the child had ever had tuberculosis even to a new general practitioner: "Why should I tell him—let him find out for himself."

Ostracism

In some families the attempt to keep the illness a secret from the neighbourhood had been the response to most painful experiences of ostracism and of consequent loneliness and isolation. The popular feeling that tuberculosis is a result of neglect, poverty, uncleanliness, and therefore a very shameful disease, as well as the tremendous fear of infection, resulted in cases of what seem to have been really cruel behaviour. One boy, who was 6 years old on his return from the sanatorium and did not go to school until 18 months later when he was perfectly well, had found that at school no other child would play with him. He was shunned equally by the children in his street. He was told by the mother of a little girl in his school that he must not breathe in her face, and several children, at their parents' request, were not allowed to sit next to him. He also started at a Sunday school at about the same time, but two children told him that if he continued to go to Sunday school they would have to have the windows open all the time. The parents did not send him there after that. On his eighth birthday his mother invited some children to tea, but none came. They have not attempted to give parties for him since.

Stories of ostracism of this kind in cases where there was no longer the slightest risk of infection were not infrequent. Whether true or exaggerated, the result had been that some families felt themselves to be outcasts and became determined to keep their past illness a guilty secret. Having themselves experienced such ostracism, too, families often found that they had not the heart to take necessary precautions against the very real risks of infection by a member of their own family. For instance, one woman said that she used to take her small child to see her own ill sister as the latter adored the baby and "it would have been too cruel to keep the baby away from her."

It is perhaps of interest that many of the attitudes and feelings that struck the psychiatric social worker when visiting these families are noted also as the characteristics of children between 6 and 13 years suffering from tuberculosis and in hospital (Dubo, 1950). Dubo noted, among other findings, their intense anxiety and preoccupation with thoughts of death, their attempts at denial, the feeling of being different from other people and stigmatized, and their tendency to take personal responsibility for the illness. She concludes that there is a need for psychotherapy as part of the treatment programme.

Conclusion

Although a tremendous amount has already been achieved in combating it, tuberculosis remains the most important infectious disease at the present time. The close interrelation between adverse socio-economic conditions and incidence and course of the illness has long been recognized, and much has been done in the last decades to improve economic conditions for the tuberculous patient. That a great deal more remains to be done is testified by the enormous case load each welfare officer in a chest clinic still has to carry, these cases being primarily those of families where there is still an urgent need to ameliorate material and economic hardships.

From a psychiatric point of view a number of studies have been made relating tuberculosis to temperament or personality type, either from the point of view of the effects of suffering from tuberculosis on the patient's personality, or of the effects of the patient's personality on the incidence and course of the illness—for example, Wittkower (1949). There appears to be a paucity of studies, however, on the effects of the illness on the patient's social relationships, whether within the family or with the community outside. What struck us so forcibly in this inquiry were the extent of the social and emotional problems resulting from a tuberculous illness in a family, the complexity of the feelings and attitudes aroused, and in particular the tremendous need found in so many of these families to talk about their anxieties. It seemed almost as if this had been their first opportunity for a long time to do so to someone who was prepared to listen at length.

In view of the pressing needs for more preventive work, medical care, sanatorium beds, better housing, and more financial assistance, it may seem premature to ask that help be given to tuberculous families for their emotional and social problems. Yet we believe that these needs will have to be met in future, both for the sake of the families themselves and for that of the community. Not only is there much unhappiness which could be alleviated, but, because of the seriousness of the disease, very strong feelings are aroused which in many cases, instead of leading to wise action, lead the sufferer to behaviour which makes matters worse for himself and others. The more aware health workers of all professions are of such feelings and the greater their skill in handling them, the more effective their work is likely to be as regards both health education and case work with individual families.

The observations reported in this paper were made in the course of a research project sponsored initially by the Sir Halley Stewart Trust and later by the Central Middlesex Group Hospital Management Committee (which manages the Tavistock Clinic) and the International Children's Centre, Paris, for all of whose support we are grateful. We are particularly indebted to Dr. J. C. Roberts and the staff of Harefield Hospital and to the regional hospital boards and county council staffs of the chest clinics which serve the County of Middlesex, for their co-operation in the inquiry, and to Mr. James Robertson, of the Tavistock Clinic, who assisted us in it.

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FATAL AGRANULOCYTOSIS DURING TREATMENT WITH CHLORPROMAZINE

BY

J. R. TASKER, M.D., M.R.C.P.

Consultant Physician, Northampton General Hospital

Although only recently introduced, chlorpromazine is already a widely prescribed drug. Serious complications encountered during its use should therefore be made known. The aim of this note is to record the clinical details of a patient who died of agranulocytosis during a course of treatment with chlorpromazine.

Literature

Mild and transient leucopenia during the early weeks of treatment with this drug is well recognized (Andersen, 1954), but fully developed agranulocytosis has seldom been recorded. Lomas (1954) drew attention to a 69-year-old woman who developed agranulocytosis after receiving 6 g. of chlorpromazine in 41 days. The total leucocyte count fell to 680 per c.mm., of which only 11% were polymorphs. The drug was withdrawn and prophylactic penicillin was administered, but after 10 days there was still no improvement in the blood count. The patient was then given five injections of 50 mg. of cortisone. Subsequently the white blood count rapidly became normal. A second case was reported from Denmark by Munch-Petersen (1954). His patient was a 71-year-old woman who was given 10.6 g. of chlorpromazine in 48 days. On the 46th day of treatment she developed diarrhoea and on the 48th her temperature rose. The white-cell count was 800 per c.mm., of which 14% were polymorphs. The patient was treated with repeated blood transfusions, folic acid, and prophylactic penicillin. In spite of a mild bilateral bronchopneumonia she made slow but steady progress, and nine days after the initial blood examination the white-cell count was again normal. A third example has been recorded in Norway by Giacobini and Lassenius (1954) in a 57-year-old woman who was treated with a combination of chlorpromazine and promethazine. The latter antihistaminic drug was used to enhance the sedative effect of chlorpromazine and to guard against any untoward sensitivity reactions. This latter device was notably unsuccessful. On the 40th day of treatment the patient complained of pain in the limbs and lassitude, and on the 45th day a blood count showed 900 leucocytes per c.mm., of which 200 (22%) were polymorphonuclears. The patient was treated with blood transfusion and penicillin, and recovered well. A fortnight after the discovery of agranulocytosis no abnormality could be found in the white-cell count.

All these patients were women, all were of middle or old age, and all recovered. All developed agranulocytosis at about the sixth week of treatment with chlorpromazine, and in none were there any warning signs of sensitivity to the drug. The patient described below differs from them in that she was a young woman, her illness proved fatal, and clear-cut clinical evidence of sensitivity to chlorpromazine preceded the development of agranulocytosis by an interval of 2½ weeks.

Case History

The patient was a married woman aged 38. She had first consulted a psychiatrist in 1943, when she was 27. A diagnosis of hysteria was made, and she subsequently attended the psychiatric out-patient department fairly regularly for a number of years. Her symptoms during this time were very numerous, and no organic cause for them could be found. They did not improve. In 1951 she was admitted to hospital in an hallucinated and maniacal state, which necessitated her early transfer to a mental hospital. There was little or no response to a course of electric convulsion therapy, and she ultimately returned home. Between 1951 and 1954 she complained frequently of lassitude, syncope, excessive menstrual loss, and pain involving most parts of the body. These symptoms could be temporarily controlled only by frequent changes in treatment. Many remedies were therefore used. They included compound tablets of codeine; sodium salicylate and potassium citrate in simple mixtures; aspirin, phenacetin, and caffeine tablets; "hypon" tablets; and "amenorone" tablets. None of these preparations is known to depress the activity of the bone marrow. Amidopyrine and the sulphonamides were not used.

On August 17, 1954, treatment with chlorpromazine was recommended. The initial dose was 25 mg. three times daily, and this was doubled nine days later, the patient receiving 150 mg. daily on and after August 26. On August 28 she complained of lassitude and fever, and her temperature was 101.2° F. (38.4° C.). Although examination revealed no obvious cause for the fever it was thought best to treat her with procaine penicillin intramuscularly for three days. The fever lasted only two days. On September 1, however, 14 days after the treatment with chlorpromazine had started, she complained that she was passing pale faeces and dark urine. Jaundice was confirmed on clinical examination. Like the fever, this also was short-lived, and on September 4 was barely discernible. On September 6 a third complication arose: an irritating rash developed on the limbs. Two days later the presence of a discrete maculo-papular erythema was confirmed: it involved all four limbs, but particularly the thighs and calves. On September 10 the rash had gone. Up to this point treatment with 150 mg. of chlorpromazine daily had been continued without interruption. It was now continued throughout 2½ weeks of relatively good health. On September 27, however, after receiving 5.475 g. of chlorpromazine in 41 days, the patient developed ulceration of the gums and tongue and her temperature rose to 101.2° F. (38.4° C.). An immediate blood count showed 900 white cells per c.mm. (polymorphonuclear leucocytes 10%, lymphocytes 90%). A diagnosis of agranulocytosis was made. Treatment with chlorpromazine was stopped at once, and the patient was immediately admitted to hospital.

On admission the patient lay still and resented examination. Her temperature was 100° F. (37.8° C.), pulse 100, and respirations 22. Her tongue was dry and furred. There were numerous small ulcers on the mucous membranes of her tongue and pharynx. The gums were also ulcerated. There was no pallor of the mucous membranes, and no jaundice, rash, oedema, or enlargement of the lymphatic glands. The heart and lungs were normal; the liver and spleen could not be felt; and the urine contained neither albumin nor sugar.

In spite of the withdrawal of chlorpromazine and the prophylactic injection of 500,000 units of penicillin intramuscularly twice daily, the patient did not improve. An irregular fever between 99 and 101° F. (37.2 and 38.3° C.) was maintained, and ulcerative stomatitis persisted. Daily blood counts, the results of which are given below, showed a persistent grave granulopenia.

Date	Hb %	R.B.C. per c.mm.	W.B.C. per c.mm.	Polymorphs %	Platelets per c.mm.
27/9/54			900	10	
28/9/54	83		1,600	10	
29/9/54	83	3,800,000	1,500		
1/10/54			1,400		
2/10/54	70		900	15	290,000
4/10/54			800	5	

On October 2 profuse diarrhoea developed, and from this point the patient rapidly deteriorated. Next day she developed right lower lobar pneumonia which failed to respond to 2,000,000 units of penicillin intramuscularly, 500 mg. of oxytetracycline intravenously, and 2 g. of oxytetracycline

intramuscularly, all given within 24 hours. On October 4, one week after admission to hospital and seven weeks after starting treatment with chlorpromazine, the patient died. Permission for necropsy was not granted.

Comment

For two reasons it is difficult to avoid the conclusion that chlorpromazine was responsible for this fatal agranulocytosis. Firstly, the agranulocytosis developed six weeks after the first dose of chlorpromazine; this interval corresponds with that noted in other recorded cases. Secondly, the agranulocytosis followed definite evidence of sensitivity to chlorpromazine. Transient fever, jaundice, and skin rashes are well recognized as complications of treatment with chlorpromazine. The other drugs used before treatment with chlorpromazine began can scarcely be incriminated. They do not carry the reputation of toxicity towards the bone marrow, and they had been taken frequently and harmlessly by this same patient on previous occasions.

This case suggests that evidence of sensitivity to chlorpromazine should be treated with respect. Fever, jaundice, and skin eruptions during the early weeks of treatment should be taken as danger signals and should compel repeated examination of the blood, if not withdrawal of the drug. Ulcerative stomatitis, particularly if it occurs at about the sixth week of treatment, should be an absolute indication for the immediate cessation of chlorpromazine therapy.

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CYST FORMATION SEVEN YEARS AFTER A CUTIS GRAFT REPAIR OF HERNIA

BY

A. G. RUTTER, F.R.C.S.Ed.

Consultant Surgeon, Queen Mary's Hospital, Roehampton

The use of skin in the repair of hernia was suggested more than forty years ago in Germany (Loewe, 1913), and was first applied clinically to post-operative incisional herniae (Rehn, 1914). It did not come into any general use for inguinal herniorrhaphy until Mair (1945) published his paper. The possibility of cyst formation due to the persistence of epithelial or glandular elements was not noted in the first two series of cases published (Mair, 1946; Marsden, 1948), but was stressed by Strahan (1950) in a series of 413 cases. Strahan found nine definite cases of cyst or sinus formation, with a number of others in which the presence of a cyst was suspected but not proved by actual operation. Most of the cysts in Strahan's series were small; but two were large, and his Case 3 is very similar to the one reported here.

Case Report

A railway worker aged 48 first developed a left inguinal hernia in 1946. The hernia was operated on in May, 1947, and the transcript of the rather brief operation note reads as follows: "Left inguinal incision. Poor musculature. Direct inguinal hernia. Cutis graft repair performed. Patient to remain in bed three weeks." The patient stated that he had made an uncomplicated recovery after operation, and that he had not returned to his job, which entailed heavy lifting, until August, 1947. He remained quite free from symptoms and from any sign of recurrence until June, 1954—more than seven years after the operation—when he began to complain of pain in the groin, radiating into the testicle, and later noticed a swelling under his operation scar. He was examined by a surgeon, who diagnosed recurrent left inguinal hernia.

Examination showed a heavily built overweight man with protuberant abdominal wall rather heavily laden with fat. There was a well-healed oblique operation scar in the left inguinal region, and beneath it an elongated smooth solid swelling lying in the long axis of the inguinal canal. It was not reducible, but appeared to have some impulse on coughing. A diagnosis of incarcerated omentum in a recurrent hernial sac was made—the details of the previous operation being overlooked through an over-hasty perusal of a rather illegibly written case record.

At operation the first feature noticeable was the unusually dense fibrotic obliteration of the normal layers of the inguinal musculature. The swelling was obviously solid, and, after it had been separated from the spermatic cord and dissected up, it became apparent that it stopped short

at the internal ring and had no communication with the peritoneal cavity. The swelling, which measured 7 cm. in length and nearly 3 cm. in greatest diameter, was removed intact. Its removal left a potential weakness in the posterior wall of the inguinal canal, which was repaired with silk sutures after a relaxing incision in the anterior rectus sheath.

The patient made an uncomplicated recovery after operation, and left hospital with no evidence of any recurrent herniation.

The swelling, when examined after removal, proved to be a cyst, with walls varying from 2 to 5 mm. in thickness. It contained a waxy inspissated material, and several dark hairs, one of which was an inch (2.5 cm.) in length, were seen lying free in it. Histological examination of the cyst wall showed a well-formed squamous epithelial lining, with a connective-tissue backing resembling normal dermis, though without its papillary structure. The size and shape of the cyst are well shown in the photograph.

Comment

Apart from the cases mentioned by Strahan in his large series, only two cases have been reported in this country of cyst formation after buried skin-graft operations (Clarke, 1952; Powell and Ewing, 1952). Clarke made a thorough review of the relevant literature, and discussed the factors favouring cyst formation. His case, however, like most of the others, was a small cyst discovered coincidently at operation for recurrent hernia. The possibility of the persistence of buried glandular elements was recognized by Rehn in his original paper. Experimental work by Zimches (1931) showed that a piece of skin inserted free into muscle tissue tends to curl up into a U shape and regularly to form an inclusion cyst; and even if sutured into position

under normal tension the epithelium may grow over the opposing surfaces and so form a cyst. This work was confirmed by Uihlein (1939), and all subsequent writers on the subject have emphasized the necessity of suturing the graft under as great a tension as possible—in contradiction of all the accepted rules for hernia repair. It is obvious, however, that this is a factor which cannot be controlled with complete certainty, and Strahan concluded that, in spite of the most careful technique, any surgeon doing a large number of these operations will inevitably meet some cases of cyst formation. Whilst this does not condemn the method, it must temper enthusiasm for it.

The present case is of interest for the large size of the cyst, requiring operative removal although the hernia itself had not recurred, and for the long interval of seven years between the implanting of the graft and the appearance of the cyst.

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Medical Memoranda

Caeco-colic Intussusception Complicating Perforated Appendicitis

The association of caeco-colic intussusception with acute appendicitis seems to be rare, only one case having been found in the literature.

CASE REPORT

A boy aged 22 months was admitted to hospital on January 24, 1954, with a history that 48 hours previously he had had abdominal pain and had vomited once. After a few hours the pain went away, but it recurred 24 hours later, and there had been periods of screaming with evident abdominal pain and pulling up of the legs, and usually a vomit. The attacks lasted for 5–15 minutes and occurred every hour or so. Between the attacks he was quiet, and in the few hours before admission became rather drowsy and disinterested. He had been taking fluids fairly well between the attacks.

Examination showed a flushed and toxic-looking little boy. His pulse was 160 and temperature 101° F. (38.3° C.). The tongue was coated, but there was no evidence of dehydration. The abdomen showed generalized rigidity, maximal on the right side, where there was extreme tenderness. Rectal examination revealed a "bogginess" in the recto-vesical pouch but no blood. The chest and C.V.S. showed nothing abnormal. A diagnosis of peritonitis from appendicitis was made, although the recent history suggested an intussusception.

Operation.—Under anaesthesia a rather bulky, sausage-shaped mass was felt just to the right of and above the umbilicus. On laparotomy through a right paramedian incision a diffusing peritonitis was found and an amount of thin pus with small fibrin flakes was sucked out. The small gut was only slightly distended. The apex of the intussusception had reach the right transverse colon; it was pushed back and easily reduced. The apex was caecal, at the level of the appendicular base, which could not be seen, as the proximal half of the appendix was retroperitoneal. This part of the caecum was thickened and congested and the appearances extended back along 4 in. (10 cm.) of ileum, the mesentery of which was rather bruised. The distal 1½ in. (3.8 cm.) of the appendix, which was visible, was congested correspondingly, and it was obvious that all this gut was fully viable. Over the area of the appendicular base was a small yellow patch, and on following the appendix back to its base by opening the peritoneum a small abscess surrounding a gangrenous perforated segment was revealed. The base was just clear, and appendicectomy was carried out. A small drain was inserted down to the area and the abdomen was closed.

Post-operatively the patient took fluids orally and was given penicillin and streptomycin by intramuscular injection, and after a slow first 24 hours he made a rapid and completely uneventful recovery. He was discharged twelve days later.

COMMENT

The clinical picture was interesting in that the recent history suggested intussusception, whereas the examination suggested peritonitis from appendicitis. The clear viability of all tissue except the perforated gangrenous segment of the appendix confirms that the appendicitis preceded the intussusception. It obviously must have done, otherwise there would have been no peritonitis. The presence of a localized abscess on the caecal wall initiated the intussusception.

It was remarkable how innocent the visible portion of the appendix looked, and this case may serve to emphasize that the appendix should be closely examined, especially where the apex of an intussusception is caecal. A small caecal abscess as an initiating mechanism was noted by Gavin Cleland (1953), but under different circumstances—*following* appendicectomy with invagination of the stump. Lipin and Miller (1948) reported a case of acute appendicitis complicated by intussusception in a man aged 21.

I wish to thank Mr. John Talbot for the opportunity of dealing with this case.

BLAIR A. THOMPSON, M.B., F.R.C.S.Ed.,
Senior Surgical Registrar, Harold Wood Hospital, Essex.

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Recovery after Penetrating Wound of the Heart

Contrary to the accepted belief of the popular fiction writer, injury to the heart by a penetrating wound of the chest may occur without an inevitably fatal result. The following is a report of a case which came under my care.

CASE REPORT

On April 2, 1953, at about 10.30 p.m., a man of 22 was brought into the General Hospital, Ashton-under-Lyne, following a knife injury sustained during a brawl. He was extremely shocked and suffering from extensive blood loss. His clothing was heavily bloodstained and small cuts were present in his overcoat, jacket, and shirt in the left precordial region. He was semiconscious and irritable, and needed considerable restraint to prevent him falling from the stretcher. Respiration was deep and sighing, there was extreme pallor of the lips, face, and hands; sweating was profuse, and no pulse was discernible at the wrist or in the neck.

After a slow blood transfusion the blood pressure rose to 56 mm. Hg, and it was decided to remove his clothing and examine his chest. There was a vertical incised wound in the fifth left intercostal space, about 1 in. (2.5 cm.) in length and 1 in. lateral to the mid-clavicular line. The wound was not now bleeding. Percussion revealed a stony dullness over the left half of the chest, with considerable mediastinal shift to the right. On auscultation no breath sounds could be heard on the left side of the thorax. A diagnosis of haemothorax was made, probably with injury to the left lung. When the systolic blood pressure had risen to 110 mm. Hg preparations were made for an emergency thoracotomy. However, on arrival at the theatre the blood pressure had fallen to 45 mm. and further resuscitation and transfusion were necessary before the operation could be started.

An incision was made along the line of the fifth rib and costal cartilage, from the mid-sternal to the mid-axillary line. On exposure of the rib, it was seen that the fifth costal cartilage had been severed close to the costo-chondral junction and the parietal pleura was open for about 1¾ in. (4.4 cm.) vertically. The rib and cartilage were excised subperiosteally from sternum to posterior axillary line, and the bed of the rib was incised medially and laterally from the edges of the original wound. After spreading the other ribs to open the wound, it could be seen that the left side of the thorax was occupied by a large quantity of blood clot, obscuring the viscera completely. About 3 pints (1.7 litres) of clot and blood-stained fluid were removed. No evidence of injury to the lung could be found; but a blood clot was protruding through a wound in the pericardium about 1½ in. (3.8 cm.) long on the anterior aspect close to the left border. The opening was enlarged to form an L-shaped flap, which was turned back, and the clots were removed from the pericardial cavity. This rendered the heart visible, and it was seen that ½ in. (1.3 cm.) lateral to the anterior coronary vessels, towards the left border of the heart, there was an incised wound lying in the length of its fibres and about 1½ in. (3 cm.) long. No blood was issuing from this wound and no attempt was made to separate the wound edges, which had adhered to each other. Five interrupted sutures of size 0 chromic catgut were inserted deeply, using each suture as a stay whilst inserting the next stitch, before cutting the ends. As much of the remaining clot as possible was removed from the pericardial space and the pericardium was closed loosely with 00 chromic gut. After further careful inspection the thorax was closed in layers without drainage, the left lung being inflated by the anaesthetist. The patient was then returned to the ward, and at that time his systolic blood pressure was 96 mm.

The following evening the mediastinum had deviated to the right and respiration was becoming laboured. There was dullness at the left base and both lungs were moist to auscultation. Aspiration of the left side of the chest yielded 10 oz. (280 ml.) of heavily blood-stained fluid. A similar aspiration after a further 24 hours yielded 12 oz. (340 ml.) of fluid, not so heavily blood-stained. No further aspirations were necessary, but an attempt was made to regulate the transfusion so that the blood pressure remained at about 100 mm.

The patient made an uneventful recovery and was discharged from hospital four weeks after admission. When seen six weeks later his only complaint was pain at the left base on coughing. There was no dyspnoea on moderate exertion.

I wish to thank Mr. P. W. Bleasedale for permission to publish this case; also the anaesthetist, without whom the operation would have been impossible. Last, but by no means least, I thank the nursing staff and laboratory technicians of the hospital.

R. W. LAWRIE, M.R.C.S.

A Case of Acute Nephritis in Pregnancy

Acute nephritis occurring during pregnancy is said to be rare. O'Dwyer and Montgomery (1954) reported three cases, and state that a search of the literature yielded only a further 23 cases. They suggest that with conservative treatment the course of acute nephritis is not adversely affected by pregnancy.

The following case of acute nephritis occurring in the fourth month of a second pregnancy is reported. The pregnancy resulted in normal delivery at term and apparent recovery of the mother. This was followed two years later by a third successful and normal pregnancy and delivery.

CASE REPORT

A 2-gravida aged 31 was first seen at the antenatal clinic on August 28, 1951, when three months pregnant. Her first pregnancy in 1945 had been normal. Her general condition was satisfactory. The urine contained no albumin, the blood pressure was 130/70, and the haemoglobin 84% (12.5 g.). She attended again on September 11, when her general health remained satisfactory, the urine contained no albumin, the blood pressure was 120/70, and she had gained 1 lb. (0.45 kg.) in weight. There was no oedema present at either attendance.

On September 15 she developed a sore throat which lasted for three days, but did not seek medical advice until a week later, when she first noticed the dark red colour of her urine. On September 27, after three days of complete rest in bed at home, she was admitted to hospital on account of the rapid appearance of considerable oedema.

On examination on admission she looked ill, her face was pale and distinctly puffy, and there was considerable pitting oedema of the abdominal wall, sacrum, and legs. She was in no pain. The throat appeared normal. Her temperature, heart, and lungs were normal. The pulse rate was 80–84 a minute. The blood pressure was 144/92. There was no tenderness in the abdomen or renal angles and micturition was painless. The uterus corresponded to an 18-weeks pregnancy. The urine was a smoky red, boiled nearly solid, and a catheter specimen showed a heavy deposit of albumin, 6 pus cells per 1/6 field, many red blood cells, and a few epithelial cells. No casts were reported but much amorphous debris. Culture gave a scanty growth of *Bact. coli*. A throat swab showed no β haemolytic streptococci. In the first 24 hours 55 oz. (1.6 litres) of urine was passed and the albumin present measured 2 g. per litre (Esbach).

Treatment at the outset comprised absolute rest in bed and restriction of fluids and salt. Milk, fruit drinks, and glucose were allowed, and added vitamins. During the first 14 days in hospital the urinary output remained satisfactory; the oedema slowly lessened and disappeared. The urine remained, however, smoky red, and on October 10 the albumin measured 6 g. per litre (Esbach). The haemoglobin was 54% (8.5 g.). The retinae were normal and the patient looked and felt better. The blood pressure varied from 140/88 to 148/92. During the next ten days the urine became normal in colour, the albuminuria diminished to 2.5 g. per litre (Esbach), and the blood pressure fell to 130/80. Oral iron was given and the protein in the diet was rapidly increased. She was discharged home to rest in bed on October 22. She was readmitted twice for a few days in November and again in January for reassessment.

On November 8 albuminuria was 1.5 g. per litre (Esbach) and the blood pressure 112/70, and on January 2, 1952, a catheter specimen of urine showed a faint trace of protein, and the deposit an occasional leucocyte and red cell with some epithelial cells and debris. Cultures showed no significant growth. The pregnancy proceeded normally. The blood pressure was 124/82 and haemoglobin 80%. The patient continued resting, mostly in bed, at home, on a normal diet with added vitamins and iron.

On February 26 she was normally delivered, in hospital, of a healthy 8 lb. 3 oz. (3.7 kg.) infant. The placenta appeared to be normal. At post-natal examination on April 16 she looked well, her blood pressure was 116/90, and an ordinary specimen of urine showed a faint trace of albumin.

Two years later, on March 3, 1954, after a normal pregnancy, she was normally delivered of her third child, a healthy infant weighing 8 lb. 10 oz. (3.9 kg.). Her blood pressure remained normal and was 120/70 at the sixth month, 10 days before delivery, and in the puerperium. The urine remained protein-free throughout. There was no oedema present before delivery. Post-natal examination six weeks later was normal.

I gratefully acknowledge the help given by Mr. William T. Kenny. I also thank Dr. John M. Malins, who kindly saw this case and confirmed the diagnosis of acute nephritis.

CARMICHAEL MACKIE, M.D., D.Obst.R.C.O.G.,
Medical Officer, Lucy Baldwin Maternity Hospital,
Stourport-on-Severn, Worcestershire.

REFERENCE

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Reviews

PERIPHERAL NERVE INJURIES

Peripheral Nerve Injuries. By the Nerve Injuries Committee of the Medical Research Council. Editor: H. J. Seddon. Medical Research Council Special Report Series No. 282. (Pp. 451+xvi; illustrated. 55s.) London: H.M. Stationery Office. 1954.

Early in the second world war, as a direct result of the Medical Research Council's work in the first, a Committee on Nerve Injuries was appointed. This included neurological physicians and surgeons, orthopaedic surgeons, and anatomists. Special peripheral nerve injury centres were established; the work in them was co-ordinated largely through the efforts of the late Dr. George Riddoch, and the clinical workers made their material available to anatomical, physiological, and statistical study. The results of this great work are contained in the present substantial volume. It is mainly clinical, with excellent clinical photographs, diagrams, and photomicrographs. Many of the chapters deal with the surgery and orthopaedic management of the injuries, and there are monographs on rates of regeneration, vasomotor and vascular changes, electromyography, and factors influencing functional recovery, to mention only a few of the contents.

It is in the tradition of the Medical Research Council that it makes its accurate researches available to the hospital worker in a form he can enjoy. This compendium on nerve injuries is an excellent example of that practice. The large number of contributors must be pleased to see the results of so many years of work so clearly available to a wider field. Though the study of peripheral nerve injuries is a very specialized subject, as this book shows, most of us see a few examples each year. The value of this collection of monographs will be as a source of reference to knowledge acquired when, in war, it was possible to raise this subject to the status of a specialty.

DENIS WILLIAMS.

CHEMICAL SPECIFICITY IN BIOLOGICAL INTERACTIONS

Chemical Specificity in Biological Interactions. Edited by Frank R. N. Gurd. (Pp. 234+xv; illustrated. $6.) New York: Academic Press Inc. London: Academic Books Ltd. 1954.

This is the third memoir of the University Laboratory of Physical Chemistry Related to Medicine and Public Health, Harvard University, and includes a foreword in memory of Dr. Edwin J. Cohn, Professor of Biological Chemistry at Harvard, who died suddenly on October 1, 1953, when the book was nearly ready for the printer.

This volume is largely based on a series of seminars held at Harvard during February and March, 1952. The chapters and authors are as follows: chemical specificity in biological interaction (E. J. Cohn); the effects of *x*-ray and other radiation on proteins and living tissues (S. Warren); physical and chemical properties of the steroids related to protein binding (R. B. Turner); biochemical problems of the steroid hormones (T. F. Gallagher); some studies on the active principles of the posterior pituitary gland (V. du Vigneaud); the influence of ion-exchange chromatography upon our concept of the structure of ribonucleic acid (W. E. Cohn); special problems in the formation of metal complexes (C. D. Coryell); interactions of metals with small molecules in relation to metal–protein complexes (J. Schubert); the specificity of metal complex formation (G. Schwarzenbach); the interactions of proteins with small molecules and ions (G. Scatchard, W. L. Hughes Jr., F. R. N. Gurd, and P. E. Wilcox). A short memoir of Konrad Dobriner (1902–52) by T. F. Gallagher is also included.

The treatment throughout is largely physico-chemical, and the biological aspects of the subject sometimes take second place, though Warren's chapter is an exception in this respect. The importance of metals in biological systems is already well realized, and the chapters devoted to the interaction of metals with many different types of substance, and particularly with those of biological significance, is a valuable summary of the situation in an important but diffuse subject and one that is clearly related to the title of the book. References to the original literature follow each chapter, and the volume constitutes a valuable summary of research in selected aspects of an important but limited field of biochemistry.

F. G. YOUNG.

THE THYROID GLAND

Endemic Goiter: The Adaptation of Man to Iodine Deficiency. By John B. Stanbury, M.D., Gordon L. Brownell, Ph.D., Douglas S. Riggs, M.D., Hector Perinetti, M.D., Juan Itoiz, Ph.D., and Enrique B. Del Castillo, M.D. (Pp. 209; 53 figures. 32s.) Cambridge, Massachusetts: Harvard University Press. London: Oxford University Press. 1954.

Lectures on the Thyroid. By J. H. Means, M.D. (Pp. 113; illustrated. 24s.) Cambridge, Massachusetts: Harvard University Press. London: Oxford University Press. 1954.

There is a Means Club in America, but even if there were not the name of Means would be certain of immortality. These two small books display two aspects of his genius: the first is the product of his inspiration, the second its direct secretion.

There are few places to-day where endemic goitre can be studied conveniently in its natural state, unspoiled by the well-intentioned interference of the medical profession. Means conceived the idea of sending an expedition to Mendoza in Argentina, and the first book is the result. It describes in detail our present knowledge of the metabolic pathways of iodine and the manner in which these pathways may be deflected by iodine deficiency; the effects of thyroid administration, and of the exhibition of the blocking agent methimazole and the stimulant thyrotropin. The descriptions have an admirable clarity, and if thereafter the authors stray into somewhat terrifying mathematics they succeed in making even this section clearer than the appearance of the formula-filled pages would at first suggest.

The second book is an easier one for the uninitiated to follow. It consists of a series of lectures given by Dr. Means in various medical schools in the U.S.A. and England, and succeeds in making a lot of confusing subjects readable and clear. The place of the thyroid in the endocrine system, the physiology of the thyroid, the newer treatments of thyroid disorders, the aetiology of Graves's disease, and the place of iodine in physiology are discussed with a charming discursiveness which suggests dinner-table conversation recorded by a tape machine and edited by a scholar.

The first of these books is for the specialist, but the second provides excellent reading for everybody.

RAYMOND GREENE.

PSYCHOSURGERY

Psychosurgery and the Self. By Mary Frances Robinson, Ph.D., and Walter Freeman, M.D., Ph.D., F.A.C.P. (Pp. 118+ix; $3.) New York and London: Grune and Stratton. 1954.

Prefrontal Leucotomy and Related Operations: Anatomical Aspects of Success and Failure. By Alfred Meyer, M.D.(Bonn), and Elizabeth Beck. (Pp. 60; illustrated. 10s. 6d.) Edinburgh and London: Oliver and Boyd, for the William Ramsay Henderson Trust. 1954.

Psychosurgery and the Self is the production of a non-medical psychologist to which Dr. Walter Freeman contributes a chapter. Taking up the "tremendous challenge to a psychologist"—namely, that batteries of established tests have yielded singularly little in the investigation of the personality changes that occur after operation—the author, Dr. Mary Frances Robinson, as the result of the employment of what she describes as "really three controlled interview techniques," reaches the hypothesis that "psychosurgery changes the structure of the self through reducing

the capacity for the feeling of self-continuity." An attempt is made to elucidate the concept and its implications for psychology and psychiatry. This discussion ranges over a wide field. Few would disagree with the contention that leucotomized patients tend to live to an unusual extent in the present.

Prefrontal Leucotomy and Related Operations, on the other hand, is a monograph of outstanding importance, and has the learning, clarity, and distinction to be expected of any work coming from Professor Alfred Meyer's Department of Neuropathology at the Institute of Psychiatry, Maudsley Hospital. It is based upon the study of 102 cases that came to necropsy, and gives a brilliant survey of what is known at present concerning the problem of the relevant role of quantitative and qualitative—that is, more regional—factors in producing the effects that are observed after operation: which in its turn bears upon the characteristically worded question posed by Freeman: "Do the frontal lobes function by mosaic or by mass action?"

Although Professor Meyer is too polite to say so directly, his work has been handicapped by inadequate case records. Special efforts, too, should be made to preserve the brains of leucotomized patients when they die; material invaluable for research is often wasted.

As the authors point out in the final paragraph of their conclusions: "Medial and orbital cuts are now being given a trial in many neurosurgical centres. The growing experience with these and other selective operations, particularly if in the fullness of time they should be anatomically controlled, will slowly resolve this problem of the relative role of quantitative and qualitative factors." This, from the clinical point of view, means how much to cut and where.

This monograph can be recommended without reserve.

DESMOND CURRAN.

LIVER PATHOLOGY

Pathologie du Foie: Études Cliniques et Biologiques. By Étienne Chabrol. (Pp. 214; 26 illustrations. 1,200 fr.) Paris: Masson et Cie. 1954.

This volume on the pathology of the liver is the fourth of a series on various aspects of hepatic disease written since 1941 by this distinguished French clinician. It makes no attempt at a systematic presentation, but comprises a miscellany of 23 chapters, ranging from 4 to 24 pages in length, dealing with topics as diverse as researches on biliary albumin and mucin and the evolution of the spa treatment of hepatic diseases. Despite this apparent diversity, the book retains a distinct sense of unity, partly because it is so obviously based upon the personal experience of a single individual, and partly because of the author's passionate desire to get away from the older concept of organ diseases and to present hepatic disease as only a special manifestation of a general body disturbance.

Anyone unfamiliar with the current French literature on the liver will find here much to surprise and interest him. Great claims are made for the use of antibiotics, especially aureomycin, in the treatment of various hepatic disorders, particularly infective hepatitis and cirrhosis. While appreciating that none of the antibiotics at present available has any effect upon the hepatic viruses, the author is convinced of the great importance of secondary infection and of its susceptibility to antibiotic therapy. Equally stimulating are the views expressed concerning the nature of gall-bladder pain and the role of the female hormones in its genesis, with special reference to their action upon the mucus secreted in the biliary passages.

Because of the obvious ignoring of work done outside France this book can in no sense presume to give an up-to-date presentation of our knowledge of hepatic disease. But as a record of one man's experience of over 50 years' work in both the laboratory and the clinic as the associate of many of the distinguished investigators of liver disease that France may rightly claim it can be warmly recommended.

L. E. GLYNN.

THE HOSPITAL ALMONER

Readings in the Theory and Practice of Medical Social Work. Edited by Dora Goldstine. (Pp. 344+vi; 37s. 6d.) Chicago: University of Chicago Press. London: Cambridge University Press. 1954.

Before 1948 many doctors regarded the main function of the hospital almoner to be assessment of the ability of patients to pay for their treatment. This was not a view which almoners themselves were prepared to accept. For many years they had attempted to establish a role more satisfying to themselves and more useful to patients, and the creation of the National Health Service gave them their opportunity.

For anyone who wishes to learn what almoners now consider to be the nature of their work this book by an American medical social worker (almoner) will be of value. It consists of a series of articles which deal with various aspects of medical social work in the United States, but most of the opinions expressed would probably be endorsed by almoners in this country. It seems clear that almoners now regard their most important task to be the practice of "casework" in a medical setting; but "casework" is variously defined. In one article (p. 109) its object is stated to be "to provide help to ill and disabled people with the personal problems associated with illness, its treatment and prevention"—a statement likely to be generally regarded as unexceptionable. Elsewhere (p. 112) the role of the caseworker is said to be "to help the person in trouble assess his situation, the problems and assets within himself and his environment, in order that he may capitalize on his strength and resources in moving toward maximum responsibility on his own behalf." This is the kind of service about which many doctors and some almoners are doubtful. The task of redefining the role of the hospital social worker is one which requires and merits the attention of doctors as well as of almoners.

THOMAS MCKEOWN.

EMERGENCY TOXICOLOGY

Handbook of Emergency Toxicology. By Sidney Kaye, B.S., M.Sc. (Pp. 303+xviii; 42s.) Springfield, Illinois: Charles C. Thomas. Oxford: Blackwell Scientific Publications. 1954.

Emergency toxicology—that is to say, the recognition and treatment of acute poisoning at the earliest possible moment with a view to saving life—is the keynote of Mr. Sidney Kaye's handbook, but it also contains much information of great value to those who have to deal with the after-effects of the emergency.

The various poisons are listed alphabetically, with descriptions of their properties, minimum lethal doses, toxic symptoms, and specific identification. A drawback of such a strict classification and compression is an occasional lack of clarity, especially with regard to the symptoms. These are not described in order of appearance, or in terms of their acuteness or chronicity. This applies particularly to the comparatively few industrial poisons listed. Under benzene, for instance, the consequences of long-continued chronic intoxication are not distinguished from the acute effects—rapid irregular pulse, ataxia, dizziness, etc., leading to death.

Undoubtedly the most valuable part of the book is on the analysis of specimens of urine, gastric lavage, vomitus, and blood, and of tablets and capsules. This will be of great value to laboratory investigators who have rapidly to identify and determine the toxic substances concerned. The analytical procedures, described clearly and methodically, include not only isolation by steam distillation and extraction by suitable organic solvents, but also the most modern methods of photoelectric colorimetric estimation and absorption spectrography. This affords great facility for quick reference to any suspected toxic agent.

Suggestions for therapy are backed by the authority of the medical staff of the Department of Legal Medicine, Medical College of Virginia, and make a further admirable contribution to a book which cannot fail to fill a long-felt want in the field of toxicology.

ETHEL BROWNING.

BRITISH MEDICAL JOURNAL
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CANADIAN MEDICINE

With the Toronto Meeting casting its agreeable shadows ahead, the sketch of Canadian medical history which appears in the opening pages of this issue gives a useful and in parts a picturesque background to a meeting which itself will be historic. Dr. H. E. MacDermot traces the story of medicine in Canada from the time of the early French settlers to the highly organized medical community which is now serving a nation of 15 million people stretched across the larger part of the North American continent. Canadian medicine has had its written history, notably a two-volume work covering four centuries, published in 1928, but Dr. MacDermot's selective picture, with its reference to outstanding events and personalities, is very welcome and apposite.

The history of medicine in Canada is linked with the history of the country itself. Many of the early doctors shared to the full the hardships, fatigues, and perils of the pioneers in other fields. They took their full part in the advance of settlement and civilization from the banks of the St. Lawrence to the Pacific coast, from the parallel of latitude 49° to the Arctic archipelago. Some of them, like medical men in other parts of the Commonwealth, notably South Africa and Australia, attained political as well as professional eminence and helped their country on its way to responsible government. The first president of the Canadian Medical Association when it was founded in 1867 was Dr. (afterwards Sir) Charles Tupper, who thirty years later became Prime Minister of Canada; and Sir Thomas Roddick, president of the first meeting of the British Medical Association in Canada at Montreal in 1897—indeed the first president of the Association outside the British Isles—was a member of the Federal Legislature.

From rough beginnings there has gradually been established a system of medical education and practice in Canada which is second to none. There are now twelve medical schools, the third to be founded being the University of Toronto, established 110 years ago, and in order of date preceded only by the two universities—French and English—of Montreal. It was in the University of Toronto that William Osler, himself born in Ontario, began the study of medicine, although his name is more closely associated with McGill. In the department of physiology of the same university Frederick Banting began his researches on the internal secretion of the pancreas. The contributions to medical knowledge of the Canadian medical schools and laboratories make a brilliant list. Canada has also its own medical literature, which is studied all over the world. One of the remarkable features of the earlier period, as Dr. MacDermot points out, was the prolificity of medical journals; and since the first of them in 1826—a French publication—72 journals have been established, most of which have died a natural and generally an early death. There are now 18 journals, and conspicuous among them is the *Canadian Medical Association Journal*, the editorial chair of which Dr. MacDermot, to the general regret, is shortly to relinquish.

At one time Canada had, nominally, some half-dozen Branches of the British Medical Association, but they seem never to have functioned as Branches and to have had only a paper existence. Then in 1924, on the proposal of the Council of the British Medical Association in London, the late Sir Jenner Verrall and the late Dr. Alfred Cox, then secretary, were sent as delegates to Canada, and the result of a most cordial visit was an affiliation of the two Associations. Affiliation was then a new idea, though it has since been adopted in the case of the Medical Association of South Africa and more recently the Indian Medical Association. The bond with Canada which was then formed was more of a sentimental than of a material nature, but it has proved strong and enduring over thirty years, as many such loosely knit bonds do where the British people are concerned. It has been strengthened by much two-way traffic across the Atlantic, and among Canadian visitors none has been more welcome than Dr. T. C. Routley, who will preside over the Toronto Meeting. Dr. Routley became general secretary of the Canadian Medical Association in 1921, at a time when it was in low water after the first world war. The relationship between the professions in the two countries has been further strengthened by the three previous visits of the British Medical Association to Canada—the first, as already stated, in 1897, to Montreal; the second, in 1906, to Toronto, and the third, in 1930, to Winnipeg. With the exception of the Melbourne Meeting in 1935, these are the only occasions on which the British Medical Association has left this country for its Annual Meeting.

The heritage of British institutions has left its stamp on medicine in this the oldest and largest of

the British Dominions, as it has on other aspects of Canadian life. In many respects the progress and pattern of medicine in public affairs, in science, and in education has been the same in the two countries. The ties will be further strengthened by the forthcoming meeting at Toronto, which is looked forward to on both sides of the Atlantic with high expectations.

NEW PATTERNS OF MALARIA CONTROL

The mass of detailed information now gathered on the intensive use of residual insecticides, particularly D.D.T., during the last ten years permits an appraisal of their value and limitations. The eradication of malaria had not previously been considered practicable except in small areas and under special circumstances, but soon after the introduction of the new insecticides the virtual abolition of the disease was envisaged in many places and has been effected in some. In only two areas have the vector anophelines been completely eradicated; in both the mosquito was an introduced species not indigenous to the country. The reason for the failure to eradicate vectors elsewhere is that the indigenous mosquito species probably antedated the advent of man, and, though they have since become more or less domestic in habit, a proportion of them still maintain their original association with wild animals and natural resting places. This sylvan population continues to live independently of man and inaccessible to routine control measures, but it can readily replace the domestic population when this is eliminated by insecticidal campaigns; and, by virtue of its ability to adjust to a new environment, it can become parasitic on man and a vector of malaria.[1]

A problem now causing concern is that strains of insects which originally proved susceptible to deposits of these insecticides have sometimes shown an increasing resistance to their effects, at first to D.D.T. but later to other chlorinated hydrocarbon preparations. The resistant strains are no longer susceptible to spraying of insecticides in dilutions and at intervals which are economically practicable. The development of resistance was first observed in houseflies, then in certain other insects, and some recent observations indicate its appearance in at least two anopheline species.[2-4] It probably develops as a result of natural selection and repeated sub-lethal contacts with the insecticides and is transmitted hereditarily. As to certain other anopheline species which still remain susceptible to deposits of residual insecticides in the dosages normally applied, control by residual spraying has ceased to be effective because the mosquito has changed its habits and stopped frequenting sprayed buildings.[5]

The difficulties that have arisen in residual insecticidal spraying for malaria control have made urgently necessary further intensive study of the reactions of anophelines to these chemicals if they are to go on being as valuable as they have been. The principles on which they are to be applied should also be clearly defined so far as our present knowledge allows, and Pampana[6] has recently discussed the changing strategy of malaria control. He emphasizes that malaria can be eliminated without elimination of the vector and that it is necessary to control transmission only during the lifetime of the malaria parasites inhabiting their human hosts. When all the plasmodia have died out—after a control period of three to four years for *Plasmodium falciparum* and *P. vivax*, which alone are widespread—further transmission is impossible even though anopheline vectors remain numerous; and provided the disease is not reintroduced the area will remain free of malaria. This is an important revision of an opinion previously widely held—that control by the spraying of residual insecticides had to be continued indefinitely unless the vector was eradicated. Experience has shown that elimination of indigenous malaria vectors is exceedingly difficult, and to spray residual insecticides over a long time is to risk creating an anopheline strain resistant to this method of control. Insecticidal spraying must therefore be restricted to as short a period as allows satisfactory control.

Certain conditions must be fulfilled before the spraying campaign can be safely discontinued. The first essential is the absence of malaria transmission for several years over most of the territory. In order to ensure this, no sources of infection must remain in the control area. In addition to applying the usual criteria for determining endemicity (particularly spleen and parasite rates), cases of malaria must be actively searched for, and they should be shown to be absent for at least a year before discontinuing spraying. The control campaign should be carried on thoroughly and simultaneously over as large an area as possible, which should preferably be surrounded by a zone in which malaria is absent naturally or as a result of control measures. The danger of reimporting the disease from contiguous malarious territories has to be guarded against, and if it can be arranged these areas also should undertake control campaigns simultaneously. Ideally, control should extend over a whole continent, and this objective has been adopted

[1] Logan, J. A., *The Sardinian Project*, 1953, p. 353, Baltimore.
[2] Livadas, G. A., and Georgopoulos, G., *Bull. Wld Hlth Org.*, 1953, **8**, 497.
[3] Georgopoulos, G. D., ibid., 1954, **11**, 855.
[4] Garrett-Jones, C., and Gramiccia, G., ibid., 1954, **11**, 865.
[5] Trapido, H., ibid., 1954, **11**, 885.
[6] Pampana, E. J., ibid., 1954, **11**, 513.
[7] Vincke, I. H., ibid., 1954, **11**, 785.
[8] Farinaud, M.-E., and Choumara, R., ibid., 1954, **11**, 793.

in America. The final safeguard is the introduction of measures to ensure rapid detection of any case of malaria and prompt prevention of transmission. The reintroduction of malaria into a population which as a result of control of the disease has lost its acquired immunity might lead to a grave epidemic, and if the local vector had become resistant to residual insecticidal spraying one of the most efficient and economical control measures would be ineffectual. The new pattern of campaign against malaria outlined here necessitates the organization of exceptionally thorough control programmes over very large areas comprising several territories, and entails greater expenditure than hitherto and better methods of detecting isolated cases of malaria. But it would be more effective and produce more rapid results. Though more costly for a few years, it would lift the burden of indefinitely recurrent expenditure on malaria control.

The problems raised by these new public health measures have stimulated interest in older and proved methods of control. New chemotherapeutic compounds are being tried either alone or in combination with D.D.T., and perhaps in suitable circumstances malaria may be eradicated sooner by a combination of these methods than by D.D.T. alone.[7,8] In this way it may be possible to reduce the risk of resistance developing to the insecticide or of behavioural change by the vector while at the same time avoiding the expense of the type of campaign envisaged by Pampana. Although the new insecticides create new and possibly serious problems, malariologists can devise methods of overcoming them.

E.C.T. IN PREGNANCY

Convulsion therapy is now accepted as a reliable means of terminating most attacks of endogenous depression months or years before they would remit of their own accord. The intense suffering of these patients and the constant risk of suicide justify the induction of epileptic fits not only in physically healthy subjects but, with the proper precautions, in patients who would be regarded as increased anaesthetic risks. Depressive states are not infrequent in pregnancy, yet the risk of inducing a miscarriage must have deterred many psychiatrists from giving E.C.T., and one well-known textbook of psychiatric treatment lists pregnancy as a contraindication to it.[1] Information in the literature is scanty, but it hardly supports the view that E.C.T. carries more risk of miscarriage than does a brief anaesthetic. F. B. Charatan and A. J. Oldham,[2] reporting a case and reviewing the literature (which covers only about a dozen cases), conclude that convulsions can be induced after the fourth month with little danger of miscarriage. This is consistent with our knowledge of the idiopathic epileptic fit. C. W. F. Burnett[3] found that in sixteen pregnant epileptics only one miscarriage occurred, and that was in a patient who had fallen heavily in a fit.

E.C.T. is now usually administered with thiopentone and a relaxant, and there is no reason to suppose that this procedure is more likely to harm the foetus than a brief general anaesthetic given for any other purpose. At the same time, unnecessary anaesthetics are usually avoided during pregnancy, and the number of reported cases in which E.C.T. has been successfully given is small. On inquiry of eight experienced psychiatrists, however, all but one said they had given E.C.T. during pregnancy but had hesitated to put the fact on record. Since the alternative to treatment is an intensely unhappy pregnancy, with the possibility of labour and the puerperium in a psychotic state, and since severe depression in early pregnancy is sometimes considered as justifying termination, there would appear to be slight reason for hesitation. Perhaps the greatest risk lies in anoxia due to a poor airway at the time of treatment, but with an experienced anaesthetist the risk must be small. While an adequate number of records of successful cases is being accumulated, the administration of E.C.T. in pregnancy would seem to be justified when there are strong indications for it—the same precautions being taken as with a general anaesthetic.

[1] Diethelm, O., *Treatment in Psychiatry*, 1950, Thomas, Springfield, p. 152.
[2] Charatan, F. B., and Oldham, A. J., *J. Obstet. Gynaec. Brit. Emp.*, 1954, **61**, 665.
[3] Burnett, C. W. F., ibid., 1946, **53**, 539.

MENTALLY HANDICAPPED GIRLS

What happened to 207 mentally handicapped girls after they left school has recently been studied at the department of public health and social medicine in the University of Glasgow.[1] The study covers the social and economic history, but not the medical history, of the girls for a period of six years between leaving one of the special schools for the mentally handicapped in Glasgow and the attainment of age 22.

The social background of these girls was by no means typical of Glasgow as a whole. Almost 90% of the fathers who were still alive when the girls left school could be placed in the lower ranks of the social hierarchy. About 25% of the girls suffered from some degree of speech impairment, while 12% were described as "of poor physique or having some severe physical impairment." When we add to this 31% of the girls "from homes classified as frankly 'bad'" by an experienced social worker, it will be realized that mental dullness was by no means the only handicap with which the girls left school to begin a career. By 1954, when they had reached the age of 22, 55 were already married. If the girls are divided into two groups, according to whether the school measurement of I.Q. was below or above 50, the outstanding fact emerges that all who were married were drawn from the over-50 group. However, the marriage rate of about 28% for this group compares with nearly 40% for all women of the same age in Glasgow enumerated at the 1951 census. The chance

[1] Ferguson, T., and Kerr, Agnes W., *Glasg. med. J.*, 1955, **36**, 50.

of marriage for the under-50 group can scarcely be said to exist. So far as could be ascertained the illegitimacy rate among the unmarried was about the same as in Glasgow as a whole.

The employment history of the girls shows the same remarkable dichotomy at the 50 level of recorded I.Q. None of the under-50 group had a record of five or more years in employment, while about 75% of the remainder had. The authors record the number of different jobs held by the girls, but in the absence of comparable data for normal adolescents the figures cannot be interpreted. Of those in employment when the study was made, nearly half were in occupations that would be classed as semi-skilled, but "general labouring work, often dirty, sometimes in foundries" claimed about one in five. The authors point out that in the present industrial conditions there is no lack of work in Glasgow which can be performed by educationally retarded girls. In an era of full employment their problems are social rather than economic.

Should the authors decide to publish a more extended account of their interesting survey they might provide a little more information. In the first place they give no hint of the way in which their 207 subjects were selected, beyond the fact that they had attended a special school for the mentally handicapped. They may have been all who left special schools in a specific year, or all who came within a certain range of recorded I.Q., or all for whom information could be obtained. If the last was forced upon the investigators, then clearly some warning about possible sources of bias will be needed. The tendency to parade our successes and hide our failures is not unknown. Moreover, in making comparisons, the authors do not consider the errors inherent in the sampling process. One or two rough tests suggest that they have satisfied themselves that the points of interest to which they draw attention could scarcely be ascribed to errors of this kind, but attention might well be drawn to the point in view of the small numbers in some of the groups. Finally, some of the comparisons made with Glasgow as a whole may be misleading in view of the social background of the subjects. The marriage rates set out in the study suggest that the chances of marriage for the group with I.Q. over 50 are reduced by about one-third as compared with normal subjects. It is known, however, that the average age at marriage is apt to be low if the social class is low. Had the subjects been compared with a control group drawn from the same social milieu, it seems likely that an even larger difference in the marriage rate might have been brought to light.

BLOOD COAGULATION

The one-stage prothrombin-time test, introduced by A. J. Quick,[1] is a reliable method for controlling dicoumarol therapy, despite the fact that the test is largely empirical and there is much controversy about what it actually measures. The classical theory of blood coagulation held that in the presence of optimum thromboplastin—that is, brain extract—and calcium the rate of thrombin formation depends on the concentration of prothrombin. If this were true, the one-stage prothrombin-time test would be a specific measure of prothrombin. This thesis was destroyed by the discovery of two coagulation factors, distinct from prothrombin, which play an important part in the activation of prothrombin by brain extract. Quick[2] noted that the one-stage prothrombin time of oxalated plasma became prolonged during storage, and that this abnormality was corrected by the addition of fresh plasma from which all prothrombin had been removed by a prothrombin adsorbant—for example, barium sulphate, aluminium hydroxide, or Seitz filters—but not by old serum. This factor was termed "labile factor" by Quick. Another factor which affects the one-stage prothrombin time is found in a stable form in plasma and serum, and is therefore called "stable factor." This factor is adsorbed by prothrombin adsorbants. The prolonged one-stage prothrombin time of plasma deficient only in the stable factor is corrected by the addition of prothrombin-free, normal serum. Recent evidence suggests that brain extract undergoes preliminary reactions with calcium, labile factor, and stable factor to form the complete thromboplastin, which activates prothrombin.[3–5] Thus it would appear that plasma is clotted in three stages by brain extract: (1) Brain extract + labile factor + stable factor + calcium form complete thromboplastin. (2) Prothrombin reacts with complete thromboplastin to form thrombin. (3) Fibrinogen reacts with thrombin to form fibrin. The one-stage prothrombin-time test is a measure of the time required for these three reactions. Since the concentrations of calcium and brain extract are standardized, the most important factors which influence the prothrombin time of plasma are labile factor, stable factor, and prothrombin. Quick postulates that plasma prothrombin occurs in an inactive form (prothrombogen) and an active form. He believes that in the presence of optimal calcium, brain extract, labile factor, and stable factor the one-stage test is a measure of active prothrombin, and he and Clara V. Hussey present evidence to support this view in an article at p. 934 of the *Journal* this week. Many other workers in this field would question the hypothesis.

The prolongation of the one-stage prothrombin time produced by administration of dicoumarol is due to reduction of both prothrombin and stable factor. The stable factor rapidly falls to less than 10% of normal, but prothrombin, measured by a two-stage technique, seldom falls below 40% of normal.[6] This and other evidence suggests that the reduction in stable factor may be more important than that of prothrombin in determining the one-stage prothrombin time in a patient on dicoumarol.[6]

If Russell's viper venom and lecithin are substituted for brain extract, the one-stage prothrombin-time test becomes insensitive to changes in stable factor. With this reagent the test shows prolonged prothrombin time of

[1] Quick, A. J., *J. biol. Chem.*, 1935, **109**, lxxiii.
[2] —— *Amer. J. Physiol.*, 1943, **140**, 212.
[3] Biggs, R., *et al.*, *J. Physiol. (Lond.)*, 1953, **122**, 554.
[4] Flynn, J. E., and Coon, R. W., *Amer. J. Physiol.*, 1953, **175**, 289.
[5] Owren, P. A., *et al.*, *Sang*, 1954, **25**, 752.
[6] Douglas, A. S., *Brit. med. Bull.*, 1955, **11**, 39.
[7] Jenkins, J. S., *J. clin. Path.*, 1954, **7**, 29.
[8] Rapaport, S. I., *et al.*, *Blood*, 1954, **9**, 1185.

plasma deficient in prothrombin and labile factor, but the test is normal with plasma deficient in stable factor.[7 8] In the presence of optimal labile factor, as in the plasma of a patient on dicoumarol, the one-stage prothrombin-time test with Russell's viper venom and lecithin is a roughly specific measure of prothrombin.[8] But this thromboplastic reagent has proved to be unreliable in controlling dicoumarol therapy, for serious haemorrhage may occur at a time when the one-stage prothrombin time with Russell's viper venom is only slightly prolonged. Likewise the two-stage test is not a sound method for controlling dicoumarol therapy. Thus there appears to be no correlation between the prothrombin level and the danger of haemorrhage; a reduction in stable factor, or some other coagulation factor, may be more closely related to the risk of haemorrhage during dicoumarol therapy.

Although, as Quick believes, the one-stage test may measure active prothrombin in the presence of optimum labile and stable factors, as in normal plasma, this is not necessarily true for plasma in a patient on dicoumarol, which is deficient in both prothrombin and stable factor. With such plasma the one-stage prothrombin-time test is a non-specific measure of the total coagulation defect produced by a dual deficiency of prothrombin and stable factor. For this reason the test, with brain extract, is a more reliable guide for anticoagulant therapy than methods that are more specific for prothrombin.

PSYCHOSOMATIC APPENDICITIS?

The aetiology of acute appendicitis remains unknown and its varying incidence in different social classes unexplained. At first sight this might seem one of the last conditions in which to invoke a psychosomatic explanation, but if the activities of the colon and the small intestine are influenced by stress and emotion, why not those of the appendix? In an investigation of psychological factors in ulcerative colitis in 1948, J. W. Paulley started using cases of acute appendicitis as controls. He found, however, that they were usually tense individuals with an unduly rigid outlook, and their attack of appendicitis had often been closely related in time to some family disaster or period of emotional strain. They were therefore considered unsuitable as controls after nineteen had been interviewed. He has now examined[1] a further ten consecutive patients with acute appendicitis, and claims to have found the same kind of precipitating situation in eight of the ten. A. L. Ribeiro,[2] practising in Kenya, has also recently reported fear or anxiety as a cause of appendicitis. He described four cases of negro women in whom appendicitis developed soon after they had been threatened in various ways.

As Paulley says, the records of his 29 cases (or 30 if the well-known case of King Edward VII is added) prove nothing, but they raise interesting questions. The higher incidence of acute appendicitis in the upper social grades seems to be definite. Will this turn out to be due not to differences in diet, but to the increased stress to which the more diligent and responsible members of society are exposed? Perhaps the answer will be found when surgeons take psychosomatic histories from all their patients.

[1] Paulley, J. W., *Arch. Middx Hosp.*, 1955, **5**, 35.
[2] Ribeiro, A. L., *Lancet*, March 19, 1955, p. 521.

SICKLAEMIA AND FLYING

It has long been known that in those inheriting the sickle-cell trait sickling of the red blood cells is brought about by anoxaemia. This fact is made use of in the commonly used rapid method of detecting sickling, in which a reducing solution consisting of 2% sodium metabisulphite is mixed with the suspected blood.[1] It is to be expected, therefore, that sickling in the blood of those carrying the trait will be accelerated when they are taken to high altitudes in unpressurized aircraft and that this may lead to sickling crises or other complications. Sullivan[2] first reported such a complication in an 18-year-old coloured American soldier who had sicklaemia and who in May, 1947, while on a flight across the Rocky Mountains complained of nausea and cramp-like pain in the left upper quadrant of the abdomen. The pain persisted for six days, recurred during a return journey six days later, and again persisted for several days. The patient was found to have a firm, tender mass (15 cm. in diameter) in the painful area of the abdomen. The mass regressed but little during the subsequent two months. Cooley and his colleagues[3] reported six further cases; these patients were all negroes who had flown for at least one hour in unpressurized aircraft at altitudes between 10,000 and 15,000 ft. (3,000 and 4,600 m.), and in five of them the symptoms—very much the same as those in the case already described—came on while they were crossing the Rocky Mountains en route from Korea. Splenectomy was performed in each case, and massive infarction of the spleen without major arterial thrombosis was invariably found. Conn[4] has added a further two similar cases to the series. Both the patients were negroes who had flown over the Rocky Mountains: they were treated conservatively, as Sullivan's patient was, with excellent results.

In these nine reported cases there appears to be a clear association between the occurrence of splenic infarction and anoxaemia caused by flying at a high altitude in unpressurized aircraft—the absence of pressurizing is confirmed in six of the cases and may be taken as likely in the remaining three. Findlay, Boulter, and MacGibbon[5] showed that flight at such altitudes may cause sickling of circulating red blood cells. They carried out experiments on three African volunteers bearing the sickle-cell trait who were taken in an unpressurized aircraft to 15,000 ft. (4,600 m.). No ill effects resulted, though all three had sickled red blood cells in the peripheral blood after 10–15 minutes at that altitude. Findlay and his colleagues rightly concluded that, "though flying for a short time at 15,000 feet does not necessarily induce a sickling crisis through reduction of oxygen tension, it may obviously cause an increased rate

[1] Daland, G. A., and Castle, W. B., *J. Lab. clin. Med.*, 1948, **33**, 1082.
[2] *Ann. int. Med.*, 1950, **32**, 338.
[3] *J. Amer. med. Ass.*, 1954, **154**, 111.
[4] *New Engl. J. Med.*, 1954, **251**, 417.
[5] *J. roy. Army med. Cps*, 1947, **89**, 138.
[6] *J. Amer. med. Ass.*, 1954, **156**, 955.

of sickling, and as Africans vary in the reduction of oxygen tension necessary to produce sickling it is possible that sooner or later an African will be found who will sickle when flown at 10,000 or 15,000 feet for a comparatively short time." The splenic infarction reported by the American observers appears to be a direct result of this increased rate of sickling at high altitudes. Among those who have studied such cases, there is, however, one dissenting opinion about the necessity of exposure to high altitudes. Doenges and his co-workers[6] reported splenic infarction in two negroes after flights at between only 4,000 and 6,000 ft. (1,200 and 1,800 m.). Both patients bore the sickle-cell trait, but were found to have haemoglobin C in their blood as well as haemoglobin S, and this raises the possibility that the presence of haemoglobin C may make the patient more liable to develop this complication under conditions of slight anoxaemia than does haemoglobin S.

The observation of splenic infarction in those carrying the sickle-cell trait need cause no alarm among the air-travelling negro public. Civil airlines do not normally fly unpressurized aircraft at heights greater than 7,000 ft. (2,100 m.), and at this level the condition is unlikely to develop except possibly among the rarer haemoglobin-C carriers. The smallness of the risk is emphasized by the fact that no complications of sicklaemia have yet been reported among the many thousands of negroes carried by the British Overseas Airways Corporation and its associates operating in Africa. The real importance of the observation lies in the fact that those carrying the sickle-cell trait should be excluded when personnel are being selected for piloting aircraft or for other work at considerable altitudes or under conditions of relative anoxaemia.

AMYLOIDOSIS IN RHEUMATOID ARTHRITIS

Amyloid degeneration has been recognized for just over 100 years as a serious but relatively uncommon complication of chronic suppuration and other chronic diseases, especially those associated with much breakdown of tissue such as osteomyelitis and pulmonary tuberculosis. But its incidence in rheumatoid arthritis is generally regarded as low. That this impression is probably based on inadequate necropsy investigation is suggested by the recent reports by D. L. Fingerman and F. C. Andrus[1] and by G. Teilum and A. Lindahl[2] of thirteen cases out of sixty-one and of seventeen out of twenty-eight respectively. When the five cases of J. M. Reece and T. B. Reynolds[3] are included, the published reports of generalized amyloidosis associated with rheumatoid arthritis now total ninety-seven. Two-thirds of these cases have been published in the last ten years, a testimony to the growing interest in the rheumatic diseases rather than to any change in their pathological characteristics.

The distribution of the amyloid deposits in these cases is that usually found in so-called secondary amyloidosis. The spleen, kidney, and adrenals are the organs principally affected, though the liver and lymph nodes are also frequently involved. Albuminuria is the commonest clinical feature calling attention to the onset of amyloidosis; less often splenomegaly, with or without hepatomegaly, may be the presenting sign. In most of the recent cases the Congo red test has been of help in diagnosis.

The association between rheumatoid arthritis and amyloidosis is of the greatest theoretical interest for the light it might throw on the pathogenesis of these two aetiologically obscure maladies. The work of G. Hass[4] and others has shown that chemically amyloid is closely related to the interfibrillary ground substance of connective tissue. Both are composed of glycoproteins the polysaccharide moieties of which yield on hydrolysis a hexosamine, a hexuronic acid, and acetic and sulphuric acids. As amyloid deposition occurs in the affected organs in close relationship to reticulin fibres and just outside capillary endothelium, it is essentially a deposition within the ground substance of substances closely related to it in chemical composition. This suggests that the excessive breakdown of connective tissue might release into the blood stream ground substance components in soluble form capable of precipitation elsewhere as amyloid. Experimental attempts to induce amyloidosis on these lines have consistently failed. The alternative hypothesis, put forward by G. Teilum,[5] accounts in a more satisfactory manner for the association of amyloidosis not only with rheumatoid arthritis but with the other conditions with which it is more frequently found. According to Teilum amyloidosis is the result of a perversion of the protein-synthesizing function of the reticulo-endothelial system, and especially of its pyroninophil derivatives the plasma cells and their immediate precursors. These cells are concerned with the formation of antibodies in response to antigenic stimuli, and according to this author their maintenance of this function is controlled by the antithetic actions of ascorbic acid on the one hand and adrenal corticoids on the other. The breakdown of this control in the face of persistent antigenic stimulation then results in the local deposition of amyloid. Apart from accounting for the pre-eminent distribution of amyloid in the tissues rich in reticulo-endothelial components such as the spleen and liver, it also provides a reasonable explanation for the associated abnormalities in the serum proteins. And, although the evidence for a persistent antigenic stimulus in rheumatoid arthritis is scarcely convincing, the predominant role of the plasma cell in the typical rheumatoid lesions is unquestionable.

Sir Russell Brain was re-elected President of the Royal College of Physicians of London on April 4. He was first elected President of the College in 1950.

At the meeting of the Council of the British Medical Association on April 13, Professor Norman B. Capon, of Liverpool, was presented with the Dawson Williams Memorial Prize for 1955 in recognition of his work in child health, particularly in the field of neonatal paediatrics.

[1] *Ann. rheum. Dis.*, 1943, **3**, 168.
[2] *Acta med. scand.*, 1954, **149**, 449.
[3] *Amer. J. med. Sci.*, 1954, **228**, 554.
[4] *Arch. Path. (Chicago)*, 1942, **34**, 92.
[5] *Ann. rheum. Dis.*, 1952, **11**, 119.

EMERGENCIES IN GENERAL PRACTICE

CORROSIVE POISONING

BY

J. D. P. GRAHAM, M.D., F.R.F.P.S., M.R.C.P.Ed.

Lecturer in Toxicology, Welsh National School of Medicine, Cardiff

A corrosive is a substance which causes destruction of tissue at the site of application; in dilute solution many corrosives merely have an irritant effect, but irritants may corrode at certain sites. According to this definition the effects of a corrosive should be limited to its local action, but some of them produce serious effects from absorption, so the classification is a loose one. Corrosives may be defined more accurately therefore as "substances having an acute and predominantly local action involving destruction of tissue." The speed and the destructive nature of the poisoning constitute an emergency in which early and effective treatment is essential.

Incidence

According to the Registrar-General's Statistical Reviews, corrosives are an infrequent cause of death (see Table).

Deaths from Violent Causes (England and Wales)

Year	Total	All Poisons	Corrosives
1950	18,889	3,274	184
1951	19,756	3,557	157
1952	18,802	3,666	129

A survey of 4,393 reports of post-mortem examinations conducted by the Department of Pathology in the Welsh National School of Medicine during the five years 1948–53 showed that the cause of death was by poisoning in 39 persons. Of these, one was due to carbolic acid and one to ferrous sulphate. A survey of the diagnoses made on 58,540 admissions to the three principal institutions of the United Cardiff Hospitals during 1951, 1952, and 1953 reveals that 251 cases of poisoning were treated. Of these, only nine were due to the classical corrosives taken internally, of which five were due to "lysol" or carbolic. During the same period 201 patients were treated for external burns due to hot objects—fires, electrical apparatus, heating devices, scalds, friction, irradiation, or chemicals. Only four were due to corrosives. Of a total number of 25 cases of burns and chemical injuries to the eye, 15 were due to corrosives. The Annual Report of the Chief Inspector of Factories for 1949 shows that of a total of 8,787 accidents involving the eye, 235 were due to chemicals (167 lime and cement). The precise number due to corrosives is not stated. The same source states that of 569,485 accidents in 1949, 1950, and 1951, 21,595 were due to hot liquids, molten metal, and corrosives. No detailed analysis is available.

It may be deduced from these and other sources that corrosive poisoning is not a common cause of emergency.

Corrosives Likely to be Encountered

The following are the common corrosives: (1) *Acids:* (*a*) Inorganic—hydrochloric, sulphuric, and nitric; (*b*) organic—carbolic, cresol and related products, oxalic. (2) *Alkalis:* sodium and potassium hydroxides and carbonates, lime. (3) *Other corrosives:* formaldehyde, salts of certain heavy metals, bichromates.

When taken internally the majority of poisonings are due to lysol and related products, with acid (usually hydrochloric) the next most frequent. From analyses of deaths by poisoning in England and Wales during 1950, 1951, and 1952,* it is seen that of 335 cases of corrosive poisoning 175 were due to lysol, phenol, and related products, and 59 to acid. The common source of the cresols is by purchase of disinfectant fluids. While most cases are suicidal, a few accidents occur, presumably owing to the keeping of small quantities of disinfectant in old medicine or liquor bottles (19 accidents to 156 suicides in this series). Accidents are evenly distributed between men and women, but the latter preponderate in the use of this method of self-destruction (115 women to 41 men).

Corrosive poisoning from swallowed mineral acid is much more common than that from caustic alkali, and the majority of cases are due to suicidal attempts (12 accidents to 52 suicides). Most of the accidents happen to men, and hydrochloric acid is by far the commonest agent. The same applies in the case of suicide, though the preponderance of males to females is less. The cause for this is obscure, but spirits of salts (hydrochloric acid) may be purchased from the pharmacist and kept in old bottles prior to use as a cleaning agent for glazed surfaces. Hydrochloric and sulphuric acids are widely used in industrial processes, and some may be obtained from the factory for private purposes such as soldering fluid.

Oxalic acid is less common as a corrosive agent than it used to be, but a few cases of poisoning still occur (seven suicides and one accident in the three years). The usual source is the purchase of salts of lemon, or salts of sorrel, from the pharmacist for use as a cleaning agent. The introduction of detergents may have made this poison less readily accessible.

Formalin is not a common agent, three suicides and one accident having occurred during 1950–2. It may be obtained freely for use as a hardening agent in photography, and has been used as a disinfectant for soft furnishings and other unwashable articles. It is used in the plastics and cellulose industries.

Heavy metals when ionized from dilute solutions of a salt act as astringents (blue-stone and silver-stick), but if their concentration is high they may act as corrosives. Of recent years there has been increasing concern about young children having access to ferrous sulphate tablets, which are attractive in appearance, 23 deaths from this cause being reported in the series of 335 mentioned above. Ferrous gluconate and other non-toxic iron compounds are being increasingly prescribed and the incidence of ferrous sulphate poisoning may therefore be expected to decrease. Of 6,598 children admitted as in-patients under the care of the Department of Child Health of the Welsh National School of Medicine during 1951–3, two suffered from ferrous sulphate poisoning, whereas during the seven-year period 1947–53, there were 15 cases.* A part of the syndrome results from absorption of excess iron, but a part of it is undoubtedly due to the local action on the gastro-intestinal mucosa, and perforation or late sequelae of extensive corrosion of the pyloric area of the stomach have occurred. Children who have swallowed these tablets should therefore be treated vigorously and urgently for corrosive poisoning.

When applied externally the circumstances are usually accidental, with the exception of the rare and execrable crime of vitriol throwing. Cases may be divided into two types:

(1) *Chemical Burns of the Skin.*—These are usually due to strong acid or alkali spilled or splashed at work. They are seldom severe, as the substance is easily washed off. Phenol or lysol on the skin can be removed before it does much damage. Emergencies from such causes are therefore rare.

Pharm. J., 1953, **171**, 50; 1954, **173**, 284.

*Watkins, A. G., Bray, P. T., and Gray, O. P., *British Medical Journal*, 1954, **1**, 335.

(2) *Severe Irritants and Corrosives in the Eye.*—By far the most common cause is lime burn in agricultural and building workers, the solid particles of calcium oxide adhering to and destroying tissue as a result of dehydration, and the hydroxide acting as an alkaline irritant. Accidents usually occur during the process of slaking the lime or while spreading it on fields, etc., or when applying it to walls and floors as a limewash. Cement contains 65% lime.

General Management

Certain principles apply to the management of all cases of poisoning. They apply no less to poisoning by corrosives than by barbiturates or other drugs.

1. The physician should consider each occasion on which the remote possibility of poisoning arises as urgent and make every effort to treat his patient promptly. Most of these occasions will prove to be false alarms, but the day will arrive when speed in giving attention is rewarding. Despite this urgency he must be calm, cool, and unhurried in procedure and obviously in control of the situation to an extent even greater than usual. Corrosive poisoning has a demoralizing effect on the patient's relatives and friends.

2. The first step is to safeguard respiration. Place the patient prone for fear of inhalation of vomitus. If there is any embarrassment to breathing, clear the airway and institute artificial respiration, at the same time requesting the presence of someone who can relieve you of this duty (many people have had training in first-aid methods; the police are expert). Fortunately, this urgent measure is seldom needed at first with corrosive poisoning, but may soon become important if oedema of the glottis develops. For this reason never delay unduly before sending the patient to hospital. Many patients who take fatal doses of corrosive fluids die of suffocation. Tracheotomy* may be necessary.

3. The next step is to remove such amounts of the corrosive as may be still active, or unabsorbed. In a case of external burns this may be the main treatment required; when dealing with a burn of the eye it is difficult but very necessary to be thorough. In the case of internal consumption of strong corrosives it is seldom advisable to use the stomach tube for fear of perforation. Details of gastric lavage will be given in next week's article on "Barbiturate and Aspirin Poisoning," should the physician decide to wash out the stomach.

4. The diagnosis of the probable nature of the corrosive should be established as soon as possible and the medico-legal aspect considered. This involves the questioning of relatives and attendants, the recovery and careful preservation of probable sources of the poison, and inspection of the patient.

5. The collection and preservation of specimens of vomitus and of any remaining portion of the presumed poison or of its container are important. This task may be temporarily delegated to a reliable attendant, but it is the physician's duty to supervise the matter closely. Specimens may be temporarily collected in any clean container—for example, glass jam-jars—but should subsequently be transferred to stoppered and labelled bottles.

6. It may be possible, depending on the probable diagnosis, to institute specific measures to neutralize acid or alkali or to counteract possible results from absorption of other substances. The measures so far taken can then be reviewed, and the degree of urgency in transferring the patient to hospital decided upon.

7. A brief general examination of the patient should be made at this stage and short notes prepared for future reference. If necessary, an analgesic may be administered now—for example, injection of morphine sulphate, ¼ gr. (15 mg.) for an adult—if respiration is adequate. Particular attention should be paid to the skin, lips, mouth, breath, vomitus, respiration and circulation, and the mental state.

*For details of the technique of tracheotomy see the article in this series on "Respiratory Obstruction," by Mr. Norman Jory (March 26, p. 781).

8. The nearest suitable hospital should be warned and transport arranged from the emergency ambulance service. The urgent nature of the case should be emphasized if necessary. Oxygen may be needed for the maintenance of respiration during the journey to hospital.

Diagnosis and Emergency Treatment of Individual Syndromes

The principal aid to diagnosis is the history and circumstances of the case. The clinical picture may be helpful, as follows.

Lysol, Phenol, Cresolic Preparations

The patient may have complained of a hot burning taste and severe internal pain, but not for long, as phenol produces a surface analgesia. Vomiting may not occur, or only once. The effects of absorption appear quickly—a few minutes to half an hour—with giddiness, delirium, and perhaps convulsions and coma. The patient is often found in this latter state. The breathing is stertorous, and the pupils are constricted; the mouth is burned dull white with phenol and the lips and chin are stained dark, while with lysol and other cresolic preparations the mouth is burned dark brown. There is usually a characteristic odour. If the physician has reached the case within fifteen minutes of the occurrence he may wish to pass a stomach tube and wash out. The addition of half an ounce (15 g.) of magnesium sulphate or a pint (570 ml.) of milk to the washing water is advantageous. Above all, guard the respiration by placing the patient prone and clearing the throat. Administer 100 mg. of leptazol subcutaneously, or 0.5 g. nikethamide intramuscularly, if breathing is poor; wash the external burns with soap and water, and order hot-water bottles as a simple measure to combat shock while awaiting immediate transference to hospital.

Inorganic Acids and Caustic Alkali

The patient is very collapsed, having experienced severe pain and violent vomiting almost as soon as the corrosive was swallowed. The jaw may be clenched, the mouth full of viscid mucus and shreds of tissue, white, foamy, blood-stained, or, later, coloured yellow or brown (acid). The vomitus contains altered blood and shreds of mucosa, apart from food. Hydrochloric and nitric acids produce an irritant fume and suffocation is often marked. Little can be done for it, as the air passages are affected. The skin around the mouth may be burned brown (acid) or white and soapy (alkali). The mind remains clear. Place the patient prone; clear the throat; do not use a stomach tube. For acid burns, endeavour to give sips of "milk of magnesia," if available, diluted 50% with water; chalk, or any gastric antacid, or dilute toilet soap in water; or the whites of two eggs in a pint (570 ml.) of water; or, if none of these is available, weak sodium bicarbonate (one teaspoonful to one pint (570 ml.) of water). The danger of the latter is the violent evolution of gas. For alkali give one part of domestic vinegar to three parts of water. Administer ¼ gr. (10 mg.) of morphine and 1/100 gr. (0.6 mg.) of atropine intramuscularly. If oxygen is available, administer it. Keep the patient warm, and give 0.5 g. of nikethamide intramuscularly if the circulation is failing. Send the patient to hospital as soon as possible.

External burns should be well washed with soap and water (acid) or diluted vinegar (alkali), and dressed with weak solution of bicarbonate (acid) or saline (alkali), and the patient transferred to hospital for further treatment. To prevent subsequent infection an injection of 300,000 units of procaine benzylpenicillin with 100,000 units of benzylpenicillin *B.P.* may be given with advantage.

Oxalic Acid and Oxalate

These have a rapid double action—immediate corrosion and subsequent depression of the heart and nervous system. A concentrated solution has similar effects to the inorganic acids, giving rise to pain, vomiting of altered blood,

suffocation, shock, and collapse. If the solution is less concentrated or salts of sorrel have been used, vomiting may be delayed, in which case the stomach should be washed out as soon as possible. Send to the nearest pharmacy for a pint (570 ml.) of lime-water, dilute it with an equal quantity of water and use it as the washing fluid, leaving the last half-pint (280 ml.) in the stomach. If a washout is not undertaken administer 4 fluid ounces (110 ml.) by mouth. If chalk is more readily available, give a teaspoonful stirred up in milk and repeat the dose three or four times. Respiratory or circulatory failure may require the injection of leptazol, 100 mg., with or without the administration of oxygen. Send the patient to hospital as soon as possible.

Formalin

Formalin causes acute pain and vomiting, and suffocation from the fumes. The stomach should be washed out with a solution of a teaspoonful of baking soda to a pint (570 ml.) of water, otherwise sodium bicarbonate should be given by mouth in warm water. Respiratory distress may require oxygen. Admit all cases to hospital, as sequelae may develop.

Ferrous Sulphate

This substance displays two actions—immediate irritation with possible corrosion, and late effects from absorption. The patient is usually a child, and the case presents with retching and vomiting, often of altered blood or mucosal shreds, pallor, tachycardia, and great drowsiness with restlessness; collapse occurs later. Hold the child upside down and tickle the fauces to promote vomiting. If gastric lavage is undertaken use a teaspoonful of sodium bicarbonate to a pint (570 ml.) of water and leave 100–250 ml. in the stomach. Guard against inhalation of vomitus, apply warmth, and send the patient to hospital.

Lime Burn of the Eye

Immediate treatment consists in vigorous washing with water poured from a jug, kettle, or tap. As blepharospasm is severe try to introduce cocaine eye-drops to facilitate this. Continue the washing for half an hour, and when the conjunctiva is cocainized inspect it carefully, everting the upper lid, and remove any adherent particles. Forceps or even fine scissors may be needed. Particularly effective in removing lime from the cornea is a solution of 2 oz. (57 g.) of ammonium tartrate in one pint (570 ml.) of distilled water, which should be kept in all first-aid rooms in workplaces where lime or cement is used. Unfortunately this solution must be used fresh. It is therefore necessary to keep the ingredients in separate bottles and to mix them immediately before use as an eyewash. When the eye has been cleaned, instil homatropine eye-drops, followed in a few minutes with liquid paraffin, cover the eye with a pad, and send the patient to an ophthalmic centre. Time spent by the practitioner on this treatment is more important than hasty evacuation of a patient who may still have lime particles in the eye.

Medico-Legal Aspects of Poisoning

If the patient dies before the arrival of the doctor or before removal to hospital, report the matter to the coroner or fiscal, who will in due course decide on the cause of death. If the patient is alive on arrival a decision must be reached whether the cause of the poisoning was accident, attempted suicide, or attempted homicide.

(*a*) If the poisoning is due to accident there is no obligation to report the matter unless the poisonous agent is one referred to in the Factories Act, 1937, administered while the patient was at work. The common corrosives are not included in the list of notifiable conditions.

(*b*) If the case is one of attempted suicide the practitioner should, in law, notify the police. However, this is an obligation which is more honoured in the breach than in the observance, and I have no knowledge of any practitioner having ever been prosecuted for failure so to do.

(*c*) If there are reasons to suspect foul play it is essential to supervise the removal of the patient to hospital. If suspicion is strong, notify the police as quickly as possible; if weak, consult the hospital authorities and let them confirm or refute. If the patient is *in extremis* and there is any reason to suspect a homicidal attempt, a dying deposition should be taken before removal. Disturb the scene as little as possible, and endeavour to ensure that no one else does so, if possible by locking up the place of death.

When the patient is transferred alive to hospital, all relevant details should be communicated by sealed letter to the medical man in attendance, especially the diagnosis of corrosive used and the treatment already given. Secure the poison container and any residues, and remove and label them. The specimens of vomitus, stomach washout, urine, etc., should be taken away in clean jars and transferred to bottles with screw tops, fixed with adhesive, and labelled with the patient's name and address, date, and nature of specimen. Lock them up in the surgery with an inventory so that they can be produced and identified if needed. Take notes at the time of the occurrence or immediately after, paying attention to the chief symptoms, the stated history, the time at which one was summoned, and the time of arrival, the alleged time at which the poison was taken, the time of death if that has occurred and is known, and any relevant statement made by the patient (in his own words). Consult the patient's medical record and make a note of any previous illness which might have some bearing on the present problem.

In the case of an external burn fairly full notes should also be taken in case of subsequent proceedings for compensation. If an accident has occurred at work, advise the patient to have the matter recorded in the "accidents book" if that has not already been done. Should death occur subsequently these notes will be needed in connexion with the inevitable coroner's or fiscal's inquiry; should the patient recover and no public inquiry ensue, the specimens may be destroyed and the notes filed with the case sheet for reference should late sequelae develop.

Next article on Emergencies in General Practice.—"Barbiturate and Aspirin Poisoning," by Dr. T. J. Thomson and Professor S. Alstead.

MODERN ASPECTS OF LIVER AND BILIARY DISEASE

[FROM A SPECIAL CORRESPONDENT]

A highly successful symposium on "Modern Aspects of Liver and Biliary Disease" was held for consultants at the Postgraduate Medical School, Hammersmith Hospital, London, from March 28 to April 1. The programme consisted of lectures, discussions, case demonstrations, films, and the demonstration of techniques used in the investigation of liver disease. It is possible to pick out only a few of the topics discussed.

Management of Jaundice

Professor N. F. MACLAGAN (Westminster Hospital) outlined the biochemical methods used in the diagnosis of liver disease. As a routine, the urine—preferably passed in the afternoon—should be examined for bilirubin, urobilinogen, and bile salts. In addition, serum bilirubin, alkaline phosphatase, and one or two of the flocculation tests should be done: he favoured the thymol turbidity and colloidal gold tests. Estimation of serum proteins and bromsulphalein excretion might give useful evidence of liver cell function. In the majority of cases these biochemical tests would confirm the clinical diagnosis.

Dr. SHEILA SHERLOCK (Postgraduate Medical School) stressed the importance of pain and pruritus, together with deep jaundice, as features of obstructive jaundice. Pruritus

was only a transient symptom in infective hepatitis, and the appearance of spider naevi suggested this diagnosis. Daily inspection of the stools was of great value in assessing the degree of obstruction, and the presence of occult blood suggested the presence of a carcinoma. In a few patients, where jaundice was prolonged or deep, a liver biopsy or even laparotomy might be necessary to establish the cause, but it was wise to wait three weeks. Treatment of infective hepatitis consisted of rest in bed until jaundice had disappeared, together with a nutritious diet. It was probably unnecessary to give excess protein or to restrict fat. Severe exertion and alcohol should be forbidden for at least six months after the attack. Obstructive jaundice which could not be relieved surgically was associated with three factors which required treating: pruritus, steatorrhoea, and a tendency to haemorrhage. Testosterone propionate given sublingually sometimes relieved itching. The patient should take a high protein, low fat diet, with large doses of calcium by mouth, and the fat-soluble vitamins, A, D, and K, should be given by injection once or twice a month.

Portal Hypertension

Dr. P. C. REYNELL (Oxford) said that the majority of cases of portal hypertension were due to obstruction within the liver—cirrhosis—or to extrahepatic obstruction of the portal venous system. A collateral circulation between the portal and systemic veins developed in the region of the oesophagus, rectum, umbilicus, diaphragm, and retroperitoneal tissues. Of these only the oesophageal vessels were important because of their liability to rupture, the other channels serving as useful means of decompressing the portal venous pressure. Splenomegaly was also a feature of portal hypertension, but occasionally the spleen could not be palpated. Haematological changes also occurred; anaemia was often due to bleeding, while leucopenia and thrombocytopenia were part of a non-specific "hypersplenism" and seldom required treatment. Haemorrhage from oesophageal varices was the most important effect of portal hypertension, and occurred in about 25% of patients with cirrhosis. It was often fatal.

Professor R. MILNES WALKER (Bristol) stressed that the only indication for surgery was the danger of serious haemorrhage. Patients with jaundice, ascites, and serum albumin levels below 3 g. per 100 ml. were bad operative risks. The new technique of splenic venography—the injection of radio-opaque dye into the spleen so as to outline the portal venous system—was of great value to the surgeon in demonstrating a patent vein for anastomosis. End-to-side porta-caval anastomosis was the operation of choice, but in patients with abnormalities of the portal vein end-to-side splenorenal anastomosis might be possible if the splenic vein was patent. Direct operations on the varices, often combined with splenectomy, were less satisfactory, but could be undertaken to control bleeding. It should be remembered that gastro-intestinal bleeding in patients with cirrhosis might be due to peptic ulceration. Thirty-five out of 42 patients who had undergone porta-caval anastomosis were well up to four and a half years after operation, and the recurrence rate of bleeding after this operation was only 5%, a much better figure than with any other form of therapy.

Ascites

Dr. R. I. S. BAYLISS (Westminster Hospital) said that two primary factors were needed for the production of ascites—namely, a lowered plasma albumin level and an increased portal venous pressure. There was abundant evidence, both clinical and experimental, that neither alone resulted in ascites. A number of secondary factors had been invoked, the most popular at present being increased adreno-cortical activity. It was well known that patients with cirrhosis and ascites retained sodium extremely avidly, the sodium content of body secretions being negligible, even on a normal salt intake. This suggested a humoral factor, and similar changes could be produced by the administration of aldosterone. Nevertheless it was possible that aldosterone is secreted in response to sodium retention. The damaged liver could not conjugate corticoids efficiently, and this might be a factor in perpetuating ascites. The part played by the antidiuretic hormone of the posterior pituitary was difficult to evaluate because of unsatisfactory methods of assay, but the patient with cirrhosis could metabolize exogenous pitressin normally. Finally, reduction in renal blood flow has been reported, and this may lead to increased reabsorption of sodium.

Dr. A. PATON (St. Thomas's Hospital) pointed out that the patient with ascites due to cirrhosis always had a poor liver, and that therefore any form of operative treatment was extremely hazardous. Surgical methods of lowering portal venous pressure had been advocated, but all had disadvantages. Talma–Morrison omentopexy and hepatopexy (the application of magnesium trisilicate to the abraded liver and diaphragm advocated by Madden) were simple operations which would increase intervals between tappings, but were probably no more effective than strict medical regimes. Porta-caval anastomosis was almost always contraindicated, and the latest operation of hepatic artery ligation unphysiological. Measures aimed at raising serum albumin were also unsatisfactory, though good results had been claimed with the use of salt-poor human albumin. However, this substance was expensive, large quantities must be given intravenously, and severe reactions had been reported. Paracentesis abdominis had many disadvantages, and should never be used as the sole means of treatment: infection, shock, a low-salt syndrome, and hepatic coma were all potential dangers, but even more important was the removal of large quantities of albumin in the ascitic fluid.

The majority of patients with ascites would respond to a strict low-salt diet, containing less than half a gramme of sodium a day, together with mercurial diuretics and 1–3 g. ammonium chloride by mouth daily. It was wise to give 1 g. potassium chloride also to make up for the loss of potassium which accompanies the diuresis. This regime might take a month or two to control ascites formation, and an initial paracentesis was often necessary. There was then a striking increase in sodium excretion in the urine and the serum albumin level rose; it might be possible eventually to relax sodium restriction. A few cirrhotics developed ascites as the result of some recognizable precipitating factor, such as alcohol, bleeding, or infections. Here treatment should be directed against the responsible factor. Another small group had intractable ascites which would not respond to the low-salt regime. These were often young patients with an "active" cirrhosis, and their prognosis was extremely bad.

Hepatic Coma

Dr. SHERLOCK discussed the neurological manifestations of liver disease, which she has termed "portal-systemic encephalopathy." The syndrome might occur in both portal cirrhosis and infective hepatitis, and recognition was important because it was often reversible and preventable. Mental changes resembled those of other organic dementias. The onset was often insidious and consisted of a change in behaviour, together with confusion and disorientation, which might be followed by stupor and coma. Patients with the syndrome had sometimes been admitted to psychiatric hospitals before the underlying liver disease was recognized. Motor disturbances consisted of a characteristic "flapping" tremor of the outstretched hands, rigidity, exaggeration of the tendon reflexes, and ankle clonus. The plantar responses were usually flexor. The tremor might spread to involve the whole body, and dysarthria and ataxia result. There was a characteristic fluctuation in the neurological features, and it was extremely rash to give a prognosis in the individual case. If the syndrome occurred in infective hepatitis it was usually rapidly progressive and the prognosis extremely bad. In portal cirrhosis, however, it might appear in a chronic form, or be precipitated by such factors as haemorrhage, operations, paracentesis abdominis, infections, alcohol, and the intake of nitrogenous substances. Hepatic coma was believed to be due to the inability of the liver to metabolize

nitrogenous compounds absorbed from the intestine, either because of poor liver-cell function or because these substances by-pass the liver through the extensive collateral circulation generally found in portal hypertension. Treatment in these cases should be directed at the precipitating factors, and in the chronic cases restriction of protein intake had proved effective.

Mr. A. G. RIDDELL (Manchester) said that normally ammonia absorbed from the gut was removed by the liver. In patients with liver disease it might get into the general circulation in the manner suggested by Dr. Sherlock. Ammonia, which was known to produce similar effects in animals, had been incriminated as the cause of hepatic coma, and certainly high blood-ammonium levels could be demonstrated in some, but by no means all, patients with hepatic coma. The syndrome could be produced by giving a high-protein diet, urea, ammonium chloride, or ammonium-containing ion exchange resins to patients with cirrhosis. It was seen also in patients who had undergone porta-caval anastomosis, about 10% developing episodes of stupor following the operation. Haemorrhage from varices was a well-known cause of hepatic coma, and it was interesting that blood introduced into the stomach of a cirrhotic would reproduce the syndrome. Treatment consisted in withholding any substance containing ammonia. Haemorrhage must be arrested as soon as possible by the use of an oesophageal balloon, and enemata should be given to remove blood from the intestines. The diet should consist largely of glucose, and chlortetracycline might help by depressing bacterial activity in the gut. Glutamic acid, either intravenously or by mouth, might be useful supportive therapy in coma following bleeding, but was of no value in the chronic syndrome or in the fulminant type associated with infective hepatitis.

Nova et Vetera

A DOCTOR IN CANADA IN 1862

In 1935 the Association held its Annual Meeting at Melbourne. Half of the party from Britain travelled via Canada and Vancouver, the other half via U.S.A. In March, 1935, the *British Medical Journal* published an account of the influence of the late Dr. W. B. Cheadle in promoting the development of Western Canada and the construction of the Canadian Pacific Railway. A correspondence which followed produced some further facts : from these sources what here follows is compiled.

Dr. W. B. Cheadle, M.D., F.R.C.P., who died full of years in 1910, was then consulting physician to St. Mary's Hospital and to the Hospital for Sick Children, Great Ormond Street, a much-esteemed London teacher and consultant. In 1862–3 he accompanied the late Viscount Milton on a buffalo-hunting expedition to the middle west of Canada. After travelling 500 miles by canoe, and more on foot, from the most westerly settlements, they wintered in a log hut, subsisting on frozen salmon and dried buffalo beef. When spring came they went further westwards, crossed the Rocky Mountains by the Tête Jaune Pass, and narrowly escaped death by starvation on the far side. Cheadle was a man of exceptional physique ; it was his strength and endurance that saved the party from disaster (he lost 41 lb. in weight during the journey). Returning to England, they published a book, which they called *The North-West Passage by Land*, describing their adventures. The title-page says it is by Viscount Milton and Dr. Cheadle, but Cheadle was actually the sole author. The book is very well written, and became a best seller : many editions were published in the next 15 years.

Cheadle was very insistent upon the potential agricultural wealth of Western Canada. He wrote : "From the Red River to the Rocky Mountains, along the banks of the Assiniboine and the fertile belt of the Saskatchewan, at least 60 million acres of the richest soil lie ready for the farmer when he shall be allowed to enter in and possess it. This glorious country, capable of sustaining an enormous population, lies utterly useless except for the support of a few Indians, and the enrichment of the shareholders" (of the Hudson's Bay Company). He pleaded strongly for the construction of a transcontinental railway, without which, he pointed out, no settler could embark on farming. Parliamentary questions were asked, both in England and in Canada ; as a result the Canadian Government sent out a commission of railway engineers, whose report disclosed no difficulties that could not be overcome. A Canadian Pacific Railway had already been advocated for some years : Cheadle's support hastened the realization of a project which would, of course, have anyhow materialized sooner or later. He is commemorated by a town named after him in Alberta. His companion, Viscount Milton, did not outlive his father, the sixth Earl FitzWilliam, and thus did not succeed to the earldom. His son was the seventh earl and his grandson was the eighth : Lady Juliet FitzWilliam is his great-granddaughter. The present (tenth) earl is a collateral relative, but not a direct descendant. A copy of the book, it may be added, is in the Association's library.

HENRY ROBINSON.

THE APPRENTICE IN MEDICINE*

A few years ago Dr. Harold Brodribb, of St. Leonards-on-Sea, showed me the indenture of his great-grandfather putting himself apprentice to William Randall, of Southampton, Apothecary and Citizen of London.† This form of indenture was used with only minor changes for at least the three hundred years after the Statute of Labourers and Artificers of 1563, and for every kind of apprentice. From the earliest recorded times young men were not considered responsible until the age of 23 years, and all technical education rested on an apprentice basis in the interval between 16 years, when the general grounding in the humanities ended, and this technical coming-of-age. Beyond the teacher–pupil relationship in the art, master and apprentice undertook towards each other mutual responsibilities in the conduct of life. The terms sound as archaic a note to-day as does the underlying philosophy of a strict contract with human behaviour as the subject. Such attempts to control the freedom of choice in others would not be tolerated in the free society of to-day: "What I do out of hours is none of your business."

This control took odd forms at times, when, for example, in 1556 no surgeon's apprentice was "to wear a beard past fifteen dayes growing upon a pain of his master's losing 6s. 8d." This was rescinded in 1557—how fascinating to know as the result of what petition, manifesto, or strike action. The master at his best taught his pupil not only technique but how he must live.

In the forties of last century references to behaviour drop out in some or are attenuated in others to teaching by the master and a promise to "obey and protect and serve" by the apprentice, although the original wording was in use at least until 1846. In some of the latest forms permission is given during the last two years to attend "such lectures and anatomical schools and hospitals as are usually commonly attended" (1851). Brodribb spent the sixth and seventh years of his apprenticeship at St. Bartholomew's, at the feet of Abernethy, Lawrence, and Stanley, although no permissive clause appears in his indenture.

In 1815, the year before Brodribb's indenture, an Act extended the sphere of influence of the Apothecaries' Society from London and seven miles beyond to the whole country, ordaining a five-year apprenticeship. This gave the Society, founded as a craft guild in 1617 as a splinter from the Grocers' Company, a chance to control and represent the general practitioner. But the leaders of the profession were college men, and college influence and the growth of universities, including London University, in the nineteenth

*Abridged version of a paper read to the Osler Club of London.
†Owing to the impossibility of reproducing the indenture clearly, only the capital initial is in facsimile.

century won the day. Real power rests, as it ever did, with those who control the register, the curriculum, and the examination. Meanwhile the apprentice system had failed to keep pace with the expansion of trades and crafts caused by the discoveries of drawing-room scientists—the eighteenth century's version of to-day's back-room boys. In 1814 an Act of Liberation allowed any man to exercise any craft or trade he pleased whether apprenticed or not, and trade apprentices began to live at home and to earn wages while training. The growth of trade unions led from time to time to restrictions of numbers and proportions of apprentices and of conditions of employment, restrictions curiously like those imposed by the guilds six or seven hundred years before.

Medicine follows these trends after the long and dignified delay that befits a learned profession. Only in recent years have the hospital resident medical staff earned a salary while serving an apprenticeship of learning at the end of training. Many of those who apply for admission to a medical school, like those who embark on the career of general practice to-day, must feel that there is now a very definite restriction of entry into the profession.

Views on the Apprentice System

Modern thought about medical education calls for a re-examination of the apprentice system. Has anything been lost that should be rescued? Walter Rivington, surgeon to the London Hospital, in his publication *The Medical Profession of the United Kingdom* (Dublin, 1888), has something to say on this point. He was a man of foresight, and advocated in those early days whole-time clinical professors and the linking of all dispensaries and hospitals with medical schools.

"Another subject is how to secure the advantages which sometimes resulted from the old system of apprenticeship? How, in other words, can certain deficiencies in hospital education be supplied? A completely qualified student brought up only at a hospital school, may be deficient in the very points which are needed for his success in practice. His 'diplomatic functions' may have been uncultivated—he may have no tact—be unable to prescribe well, have never seen cases of measles, scarlet fever, smallpox, and many children's ailments; may not know how to deal with patients, or to keep books, or to arrange a surgery. All these wants can be fully supplied by residence with a busy general practitioner, and the best period of residence is either after the end of the third year, or after obtaining a qualification to practise. We should be inclined to require every assistant to a general practitioner to have passed the proposed examination at the end of the third year. The passage of this examination should entitle a student to a certificate that he was fit to attend midwifery cases not requiring instrumental interference, and to perform those minor acts for which assistants—unqualified assistants—are required. He should not be allowed to sign death certificates; students living with practitioners before this period should be called, not assistants, but pupils. There should be no more unqualified assistants, but there should be 'certificated assistants,' and any infringement of the rules laid down as to the extent of assistance for which the certificate should be granted, should be visited with serious penalties on the general practitioner. Certificated assistants should not be permitted to manage bogus dispensaries or to carry on branch practices. . .

In this statement of 66 years ago there seems to be a foreshadowing of the pre-registration house appointment and the trainee assistant. Is it possible that these can achieve the balance, so much desired, between technical education in the science and craft of medicine and training for the life of the doctor?

Piety demands a footnote on the life of that William Perrin Brodribb (1800–69) whose apprenticeship indenture is here illustrated. He was the son of Uriah Brodribb, of Warminster, and the family had farmed their own land at Clitton, in Somerset. Henry Irving (Brodribb) was of the same family.

William Perrin, after apprenticeship to a doctor in Southampton at the age of 16, finished his training at St. Bartholomew's Hospital. He qualified M.R.C.S. (1822) and L.S.A. (1823), and these certificates are still in existence. In 1838 he moved from Southampton to 12, Bloomsbury Square, London. His second wife was Miss Aitken, daughter of a neighbouring doctor, Charles Rachemont Aitken, into whose

His Indenture witnesseth, That *Wm Perrin Brodribb Son of Uriah Brodribb of Warminster Grocer* doth put himself Apprentice to *William Randall of Southampton Apothecary & Citizen of London* to learn his Art; and with him (after the Manner of an Apprentice) to serve from the Date hereof until the full End and Term of Seven Years, from thence next following, to be fully complete and ended. During which Term, the said Apprentice his said Master faithfully shall serve, his Secrets keep, his lawful Commands every where gladly do. He shall do no Damage to his said Master, nor see it to be done of Others, but that he to his Power shall let or forthwith give Warning to his said Master of the same. He shall not waste the Goods of his said Master, nor lend them unlawfully to any. He shall not commit Fornication, nor contract Matrimony, within the said Term. He shall not play at Cards, Dice, Tables, or any other unlawful Games, whereby his said Master may have any Loss. With his own Goods or Others, during the said Term, without License of his said Master, he shall neither buy or sell. He shall not haunt Taverns or Play-houses, nor absent himself from his said Master's Service Day or Night unlawfully. But in all Things, as a faithful Apprentice he shall behave himself towards his said Master, and all his, during the said Term. And (the Sum of *Three hundred & fifteen pounds* of lawful Money of *Great Britain*, being paid or secured to the said Master, as the Consideration for taking his said Apprentice) the said Master his said Apprentice, in the same Arts which he useth, by the best Means that he can, shall teach and instruct or cause to be taught and instructed; finding to his said Apprentice, Meat, Drink, Apparel, Lodging, and all other Necessaries, according to the Custom of the City of *London*, during the said Term. And, for the true Performance of all and every of the said Covenants and Agreements, either of the said parties bindeth himself unto the other by these Presents. *In Witness* whereof, the Parties above-named to this Indenture have put their Hands and Seals, the *third* Day of *September* in the *Fifty sixth* Year of the Reign of our Sovereign Lord *George the third* by the Grace of God, of the United Kingdom of *Great Britain* and *Ireland*, King, Defender of the Faith, and in the Year of our Lord, One thousand Eight hundred and *sixteen*

Sealed and delivered (being first duly stamped) in the Presence of

S. Backler

Willm Randall

Willm Perrin Brodribb

house he later moved (No. 7, Bloomsbury Square). He had a successful private practice in this middle-class neighbourhood and he was surgeon to the Magdalen Hospital, then in Blackfriars Road. For the last seven or eight years of his life he was Secretary to the Court of Examiners of the Apothecaries Hall.

He had three sons—the first, a Fellow of St. John's College, Cambridge, later achieved fame by a translation, with Church, of Tacitus. By his second wife he had A. A. Brodribb, for many years Parliamentary Correspondent of *The Times*, and C. A. Brodribb, whose descendants carry on, without a break, the medical tradition founded by W. P. Brodribb.

I am indebted to Dr. Harold Brodribb for a photograph of the indenture and to Mr. Poynter, of the Wellcome Historical Medical Library, for gathering the indentures in that library for my inspection.

A. WHITE FRANKLIN.

Reports of Societies

PRESENT STATUS OF HYPOTHERMIA IN ANAESTHESIA

On April 1, under the chairmanship of Dr. BERNARD JOHNSON, dean of the Faculty of Anaesthetists of the Royal College of Surgeons, the Section of Anaesthetics of the Royal Society of Medicine debated the present status of induced hypothermia. The opening papers were both by anaesthetists with wide experience of this technique.

Dr. C. F. SCURR (Westminster Hospital) opened with a review of the physiological changes that accompany a general lowering of the body temperature. He pointed out that at normal body temperature tissue anoxia from circulatory arrest leads to cellular death unless rapidly relieved. In cases of cardiac arrest, for example, the heart might be restarted by massage, but often as a result of the delay the brain suffered irreversible damage. Hypothermia reduced the cell metabolism in a linear fashion so that cells could survive anoxia for longer periods. Animal experiments had shown that at a body temperature of 25° C. the circulation to the brain could be completely occluded for 20 minutes without either physiological or histological evidence of cerebral damage. Recently, Bailey had reported a case of complete circulatory interruption in a child for 22 minutes at a temperature of 21.6° C. in whom there was no evidence of cerebral damage 30 hours after operation.

Benefits and Dangers

The indications for hypothermia were fourfold, said Dr. Scurr. First, intracardiac procedures requiring an open heart, temporary occlusion of the venae cavae, and cessation of the circulation. Second, certain congenital cardiac anomalies in which there was cyanosis or the great vessels required transplantation. Third, intracranial procedures involving temporary arrest of the circulation to part of the brain : it had been suggested here that hypothermia might also increase the margin of safety of induced hypotension for neurosurgical procedures. Finally, operations or grafts to the great vessels supplying vital organs. Under normal conditions the kidney and spinal cord could barely withstand 30 minutes of circulatory arrest, but under hypothermia (27–28° C.) ischaemia of two hours' duration had been reported with only minimal—although definite—signs of transient paraplegia.

Amongst the disadvantages of the hypothermic state was the increased irritability of the myocardium which might lead to spontaneous ventricular fibrillation. The exact cause of this irritability was imperfectly understood. The evidence that ionic changes or anoxia of the myocardium were the sole cause was contradictory. A possible cause was that during hypothermia acetylcholine production was depressed, so that the pacemaker lost its dominance and ectopic foci appeared. The fact that neostigmine has a powerful protective action against ventricular fibrillation was in keeping with this theory. Most workers of experience agreed that hyperventilation, with carbon dioxide absorption, helped to reduce the incidence of cardiac irregularities during hypothermia. Nevertheless continuous electrocardiographic control was essential throughout the operation as the appearance of arrhythmias or ectopic foci was regarded as a danger signal.

Other disadvantages of hypothermia were the production of the stress response to cold and the increase in viscosity of the blood as the temperature fell.

Technique

Of the two main methods of reducing the body temperature—namely, surface cooling and the extracorporeal circulation—the surface method, using a cooling blanket, had been the most favoured at the Westminster Hospital, continued Dr. Scurr. The patient was anaesthetized with ether, cyclopropane, or thiopentone/nitrous oxide/oxygen and a muscle-relaxant to prevent shivering. The body was then wrapped in a cooling blanket, through which water circulates at 2–4° C. Before the desired temperature was reached the pump was stopped and warm water passed through the blanket. This reduced the tendency of the body temperature to continue to fall after the cooling process had ceased.

Dr. T. CECIL GRAY then described the experience of members and associates of the Liverpool Department of Anaesthesia with 110 operations under hypothermia. In the first 40 cases the technique originally described by the French authors had been used, intermittent doses of chlorpromazine, pethidine, and promethazine hydrochloride being administered. This method had now been abandoned because of the difficulty in controlling the shivering and the length of time to lower the temperature. The present method was to induce light anaesthesia with thiopentone/nitrous oxide/oxygen, prevent shivering with a muscle-relaxant (D-tubocurarine), and then give moderate doses of chlorpromazine to aid the cooling process. Surface cooling with either ice-bags or a cooling blanket was preferred. The patient's position should be changed every 15 minutes to prevent pooling of the blood, which would otherwise result in a sudden fall in the body temperature when the patient was finally moved. A colour film demonstrating the method used for cooling a patient prior to an operation for porto-caval anastomosis was then shown.

Mortality and the Reaction to Cold

Dr. Gray went on to say that he agreed in principle with Dr. Scurr's indications for hypothermia in clinical surgery, with two modifications. First, he did not think that cooling was necessary in cases of congenital heart disease undergoing a Blalock operation. Second, in general surgery it appeared to provide some protection against surgical trauma as well as permitting the use of hypotension in subjects who might otherwise be considered unsuitable for this. To date, investigation of patients undergoing hypothermia had failed to confirm the view that pituitary–adrenal responses were modified by cold. On the other hand, an investigation in animals suggested that inhibition of the stress response might account for some of the benefits of hypothermia.

In the Liverpool series there had been 13 deaths in the 110 cases. The high mortality was largely due to the nature and magnitude of the surgical procedures. There were, however, three cases of fatal pulmonary embolus in this group, which might be significant. Dr. Gray concluded by stating that hypothermia was a specialized technique which carried very definite risks, and at present it should be used only in the larger centres. Provided the temperature was not reduced below 28–30° C., the lowered metabolism and possible diminution of the stress response had proved of value in selected cases for general surgery.

Discussion

In the discussion that followed, Dr. J. W. DUNDEE (Liverpool) described a neurosurgical case in which the middle cerebral artery had been occluded for eight minutes at a body temperature of 30° C. without any signs of post-operative cerebral damage. In another case at a similar

temperature hypotension in the head-up position had been maintained for four hours without ill effect.

Dr. B. G. B. LUCAS (University College Hospital, London) stressed the difference, under hypothermia, of the heart and the brain in their tolerance of ischaemia. At normal temperature the brain was the more sensitive to ischaemia, while at temperatures of 25° C. the brain would withstand circulatory arrest for 30 minutes, whereas the heart would tolerate arrest for no longer than 15 minutes. Therefore for endocardiac surgery taking some time, either some form of coronary perfusion was necessary or much lower temperatures would have to be used.

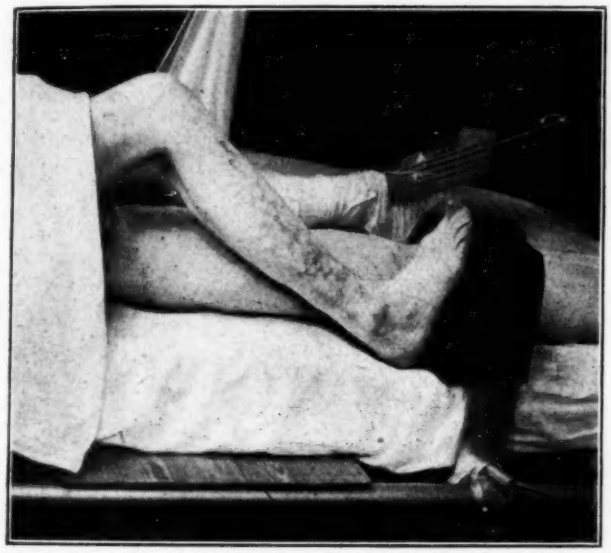
Mr. C. E. DREW (Westminster Hospital) thought that operations on children with congenital cyanotic heart disease were better done under hypothermia, as this allowed the surgeon greater freedom in choice of operative technique if some unusual malformation were encountered. It also lessened the risk of cerebral thrombosis in these patients.

Dr. G. JACKSON REES (Liverpool) thought that hypothermia should not be used for children with congenital cyanotic disease undergoing a Blalock operation, as this only increased the risk without providing any benefits. Adequate ventilation with a high percentage of oxygen was far more important.

Preparations and Appliances

BED FOOT-REST

Mr. G. T. F. BRADDOCK, orthopaedic registrar, Whittington Hospital, London, N.19, writes: The foot-rest here shown has been simply made by the hospital carpenter and the theatre technician from old orthopaedic traction fittings. This attachment fulfils the following functions: (1) It allows the patients to push themselves up in bed, and to keep themselves from sliding down the bed when traction is



applied to the other limb. (2) It encourages constant use of the good limb, and therefore reduces the tendency to thrombotic complications as well as maintaining muscle tone. (3) It prevents foot-drop. (4) It acts as a bed cradle and prevents the clothes from touching the unaffected foot. It is unnecessary to remove the foot-rest during sleep. (5) It prevents the development of a sore heel, which is very common when the patients have to push themselves up in bed with their heels. (6) It reduces the energy necessary, by the nursing staff, in lifting patients up the bed.

Patients who have had the benefit of this attachment complain bitterly if it is removed. Its use need, of course, not be confined to patients in traction. All of us who read in bed are conscious of the difficulty in keeping up.

Correspondence

Primary Aldosteronism

SIR,—Dr. J. G. Llaurado's interesting letter (*Journal*, April 2, p. 851) raises several matters requiring further explanation. Professor Conn[1] has now published a preliminary account of the first recognized case of primary aldosteronism, and ends by stating that a right adrenal cortical tumour, 4 cm. in diameter, has been excised. Information regarding the effects of the operation on the disease is awaited with great interest. This pioneer work makes it very probable that the case reported by Evans and Milne[2] as "potassium-losing nephritis" was in fact another example of primary aldosteronism. The patient has improved dramatically with medical measures alone, and is not fully convinced of the necessity of further investigation. It is hoped, however, that further investigations may become possible.

We agree with Dr. Llaurado that the two cases he quotes are probably examples of this disease, as is also the case described by Earle *et al.*[3] The reason for the emphasis on impaired renal function in all these cases is that potassium deficiency produced by primary aldosteronism or by other causes will result in a nephropathy which may closely simulate primary renal disease. Many cases have now been published[4–9] in which severe potassium deficiency has produced this nephropathy associated with vacuolization of the cytoplasm and pyknosis of the nuclei of renal tubular cells, the so-called "clear cell nephrosis." The resulting renal functional impairment has been studied by Schwartz and Relman,[9] who found a reduction of the glomerular filtration rate and renal plasma flow with complete isothenuria. These functional defects were abolished by treatment with potassium supplements. One of us[10] has shown that a corresponding defect in the urinary acidification mechanism can be produced by comparatively mild experimental potassium depletion.

So-called "potassium-losing nephritis" is certainly not invariably due to primary aldosteronism. We consider that the following points would favour a diagnosis of primary aldosteronism: (*a*) absence of definite evidence of a primary nephritis; (*b*) the need for very large potassium supplements to maintain a normal serum potassium level—in the patient of Earle *et al.*,[3] 625 mEq daily (equal to 46 g. potassium chloride) was needed to do this; (*c*) evidence of an adrenal tumour; (*d*) excretion of excess aldosterone; (*e*) renal biopsy showing the characteristic tubular lesions of potassium deficiency without evidence of primary nephritis.

At the time our joint studies were made we were unable to tell whether or not the aldosterone output was primary or secondary to the electrolyte abnormalities. As it was already accepted then that aldosterone output is increased in the nephrotic syndrome and in other oedematous states, a secondary cause for this high output seemed to ourselves and to Dr. Llaurado to be more probable. We were relieved, therefore, to observe that Dr. Llaurado does not claim any priority in the description of the syndrome of primary aldosteronism. In our opinion Professor Conn deserves full credit for his brilliant exposition of this interesting but rare new disease.—We are, etc.,

C. L. COPE.
M. D. MILNE.

London, W.12.

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Sickling and Malaria

SIR,—With reference to the recent correspondence published in the *Journal* on the subject of the possible relationship between sickling and malaria (*Journal*, November 13, 1954, p. 1162, and January 29, p. 285) may we add a brief note quoting the preliminary findings of some malariometrical indices investigated in an African child population aged between 5 and 12 years?

Of the total of 529 children recently seen in the course of two surveys in Southern and Northern Nigeria 107, or 20.2%, were showing the sickle-cell trait. The comparative results of two malariometrical indices, crude parasite rate and positive parasite density index in sicklers and non-sicklers respectively, are shown in the following tables.

TABLE I.—*Sicklers*

Age Group (Years)	No.	Crude Parasite Rate	Positive Parasite Density Index
5–7	36	64·0	2·61
8–10	38	55·2	2·29
11–15	19	68·5	1·93
Total	93	61·2	2·32

TABLE II.—*Non-sicklers*

Age Group (Years)	No.	Crude Parasite Rate	Positive Parasite Density Index
5–7	148	47·3	2·89
8–10	178	65·8	2·19
11–15	110	49·0	1·63
Total	436	55·3	2·20

The figures quoted above do not indicate any constant relationship between the two malariometrical indices and the presence of the sickling trait. In particular there is no evidence of any contrast between the positive parasite density of sicklers and non-sicklers. In the 5–7 age group the difference between the index figures of 2.89 and 2.61 corresponds to a difference of geometric means of approximately 470 and 380 parasites per cubic mm. This difference between two mean parasite densities is too small to warrant our concluding that the malaria affecting these Nigerian children differed in severity in sicklers from that seen in non-sicklers. This investigation continues now on a larger scale.—We are, etc.,

H. M. ARCHIBALD.
L. J. BRUCE-CHWATT.

Lagos, Nigeria.

Clinical Staging of Carcinoma of the Breast

SIR,—The letter by Mr. Michael Harmer (*Journal*, March 26, p. 790) must meet with the approval of all clinicians interested in the study of carcinoma of the breast. Any progress in the assessment of the results of treatment is materially hampered by inadequate clinical staging, and Mr. Harmer enumerates reasons why the breast is peculiarly suitable for a universal agreed staging.

The survey of cancer published in 1952 by the British Empire Cancer Campaign collected over 2,000 cases—nearly 30% of all the cases of cancer in the female. And the average age was in the fifties, so it is not primarily a disease of old age. In addition, various advances in treatment—especially endocrine control—have increased the relatively good survival rate even further.

But there are so many centres and so many surgeons that a simple staging seems essential. A complex staging will never succeed except in those few well-equipped and staffed centres: simplicity is the keynote, even if it can allow considerable clinical variations. If surgeons could be persuaded to indicate in the notes their estimated clinical staging at the first attendance of the patient it would save much tedious perusal of records with its consequent difficult reassessment. Prior to the war I was associated with the Clinical Research Committee of the British Empire Cancer Campaign, and more recently have followed up our cases here in Leicester. In both instances the clinical staging was the stumbling-block in the investigation, and much time was expended in sifting out the relevant clinical details. If a simple staging was adopted then it can be widely disseminated and we can start to assess results, knowing exactly that we are discussing the same problem.

I welcome Mr. Michael Harmer's initiative and wish him every success in his quest for a universal staging: for a sound basis of staging is the firmest foundation in the study of the results of treatment.—I am, etc.,

Leicester. G. C. SAWYER.

SIR,—I should like to be allowed to add a footnote to Mr. Michael Harmer's letter (*Journal*, March 26, p. 790).

There is associated with this department, which is responsible for statistical analysis of data relating to cases of cancer registered in England and Wales, a committee under the chairmanship of Dr. A. H. T. Robb-Smith which advises on cancer statistics generally and on the national registration scheme in particular. At recent meetings this committee, which is a subcommittee of the Registrar-General's Medical Advisory Committee (chairman, Sir Ernest Rock Carling), has been much concerned with the problem of establishing uniform systems of staging. Largely for the reasons enumerated by Mr. Harmer, it has selected the breast as the most suitable site for immediate study. In doing this, the committee is, of course, taking account of various existing methods of staging, including those considered at the sixth congress of the International Union against Cancer.—I am, etc.,

General Register Office, London, W.C.2. R. M. BLAIKLEY.

Manipulation and Low Back Pain

SIR,—In your recent spate of articles and correspondence on low back pain, we see a reawakening of interest in manipulation. Twenty years ago there was a flurry in the medical profession created by the success of certain bone-setters. Orthopaedic surgeons enthusiastically tried out some rather rough and ready manipulative techniques, but because the results with powerful manipulation under anaesthesia were unsatisfactory their interest waned, and in fact waxed in the opposite direction, condemning manipulation as a dangerous practice. Now, since intervertebral disk lesions are better understood, a new wave of interest has sprung up and we have an impressive array of medical men strongly advocating manipulation in the treatment of low back pains: R. Barbor, J. F. Bourdillon, L. S. Calvert, A. B. Coyer and I. H. M. Curwen, E. J. Crisp, J. Cyriax, A. C. Elkin, W. Grant Waugh, D. B. Ramsay, G. O. Tippett, W. E. Tucker, and R. W. R. Watson.

Bourdillon (*Journal*, March 19, p. 720) and Watson (*Journal*, February 12, p. 413) strongly advocate the osteopathic method of manipulation. Cyriax has claimed a method of manipulation, now so often referred to as the Cyriax technique, which is essentially derived from the osteopathic methods. Many others are striving to develop techniques of manipulation themselves. What a pity that the experience of 80 years in the art of manipulation as exhibited by the best osteopaths is not being utilized by the medical profession as a whole. It is not the fault of the osteopaths. They are there and ready to help in the training of medical men. The London College of Osteopathy has been training doctors for the past ten years, and, as we see from Cyriax's article (*Journal*, January 15, p. 140), osteopathy has become recognized in France and Switzerland, and for a long time now has been recognized in the U.S.A. Why is Britain so far behind in this matter? It is high time that we here in England appointed a committee of medical men interested in this field to get together and study the matter so that the public at large can benefit from the undoubted advantages which can accrue from the osteopathic methods of manipulation.—I am, etc.,

London, W.1. ALAN STODDARD.

Chicken-pox Quarantine

SIR,—I do not entirely agree with Dr. M. Curwen (*Journal*, March 19, p. 727) that chicken-pox is a trivial disease at all times.

Some 15 years ago I was called to attend a boy 6 years old who was suffering from chicken-pox and who was allowed to go about the house for about a week without medical attention. The parents thought it "was only chicken-pox, and the whole school had it." I was called in because the boy was walking in circles and to one side all the time, and was unduly sleepy. This case turned out to be one of encephalitis lethargica, and a consultant called in confirmed the diagnosis of encephalitis lethargica caused by the chicken-pox virus. The patient recovered, leaving sequelae of enuresis and stammering. The enuresis got better after a few years but the stammering persists to this day.

It would be interesting to know the views of fever consultants on the opinion expressed by Dr. Curwen.—I am, etc.,

London, N.9. M. P. K. MENON.

Ovariectomy and Coronary Disease

SIR,—The work of Rivin and Dimitroff,[1] Paul White,[2] and Leitner[3 4] (see Dr. Z. A. Leitner's letter, *Journal*, April 2, p. 852) is of considerable moment to the gynaecologist. This research proves that excess cholesterolaemia has an intimate connexion with coronary heart disease. If this be so, then the school of thought that maintains that every hysterectomy should include total ablation of both ovaries is annihilated, for it would appear that, quite apart from the disastrous menopausal symptoms so produced, such a patient is in imminent danger of becoming what Paul White calls a "coronary individual"—a condition which may exist until she is 60 or over. Moreover, it emphasizes the great danger of using radium or *x*-rays for fibroids, metropathia, or functional conditions. It would seem, therefore, that in addition to conserving the ovaries in all non-malignant conditions we should give very careful instruction as to the avoidance of a dietary rich in fat in such patients, for the incidence of severe coronary atherosclerosis in castrated females approximates that in males, a ratio that normally is in the region of one in ten. Indeed, this remarkable sex difference in the incidence of atherosclerosis suggests that oestrogenic hormones exert an inhibitory effect upon the pathogenesis of coronary disease.—I am, etc.,

London, W.1. V. B. GREEN-ARMYTAGE.

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Natural Childbirth

SIR,—If a woman is fortunate in being helped to have a happy, healthy pregnancy it is a pity if she expects, in this far from perfect world, to go through childbirth too without any disappointment or physical distress, and I hope no class in training for natural childbirth is led to expect absolute perfection every time. I, too, have been enthusiastic in recommending intelligent mothers to learn to help themselves by relaxation and exercises, and found this of great value in my own case. I did not have the benefit of training in a class: I had to read and practise on my own. One of my reasons for wanting to try natural childbirth was the way in which a patient, having a normal confinement in hospital, seemed to be deprived of full consciousness at a time when she could be of most use in delivering herself. Even in first-stage labour, under practically any medication, she seemed to require *more* rather than less nursing attention; I asked myself if I should not prefer full consciousness and the ability to lie quietly (though I did not know anything about relaxation then), rather than be under the influence of one of the analgesics then in use and not be sure of my even remaining *on* one of the narrow hospital beds. In my three confinements the end of the first stage was the most trying, and control was most likely to be lost then; but one knew that the second stage was not far away, with something to see for one's hard work. Incidentally, I would like to hear more nurses and doctors referring to "contractions" instead of "pains." In all fairness, it should be noted that natural childbirth is not claimed to be painless childbirth.

Some benefits, which are obviously not in doubt, are (1) increased co-operation of the patient—childbirth is not a passive event; (2) reduction of ignorance and of fear of the unknown; (3) giving of hope and a feeling of security, even when there seemed very little to feel secure about, as during the war years.—I am, etc.,

Old Cumnock, Ayrshire. MARY MACK.

SIR,—May I add a letter to the recent correspondence in the *Journal* concerning natural childbirth? I am a doctor's wife, but not medically qualified, and had my first baby seven months ago. I too was an ardent believer in Dr. Read's ideas and attended antenatal classes. The birth of my baby was a wonderful experience which I have no wish to forget. Everything went as I had been led to believe. Lest it should be thought that I was one of those women who would have had an easy time in any case, may I state that my pelvic measurements were anterior–posterior diameter 105 mm., transverse diameter 105 mm., and the head did not engage until a few hours before the actual birth, labour lasting 24 hours in all? Relaxation enabled me to wait patiently through a long first stage—the second stage lasted only 20 minutes.

I do not understand Mrs. Constance Lynn's reference (*Journal*, April 2, p. 851) to the exercises she had to do during labour, as there are none. The exercises one does throughout pregnancy are to prepare one's muscles for the hard work they will have to do during the second stage, which in my case they certainly did, as I was able to make the fullest use of my contractions. Mrs. Lynn was misled if she believed that nothing was required of her but to "contentedly await events." I was warned that labour meant what it said—hard work—and that I would experience some degree of discomfort, perhaps acute at some stage. However, my son's indignant wail as he entered the world amply rewarded my hard work. I felt no exhaustion either immediately after the birth or later.

I do feel, however, that a labouring woman needs an attendant to encourage her towards the end of the first stage, when even the best-trained mother can forget what she has been taught and lose control over her emotions. I had my husband to help me here, but I realize not all mothers are so fortunate. Perhaps a rearrangement of hospital routine which cut out the inessential jobs (is it really necessary to do five or six swabbings a day?) would leave the midwife free to do her real job of attending to the mother instead of the mother being left on her own "to get on with it."

Incidentally, I too have compared notes with other relaxation patients, the great majority of whom agree that relaxation was a wonderful help. The midwives at the hospital I attended also said that relaxation patients had easier births than other patients.—I am, etc.,

Yeovil. P. M. LEADLEY.

SIR,—It seems fair enough that doctors' wives should have their say in this correspondence. Therefore, as the mother of three children, and also as a speech therapist with some experience of teaching relaxation, I should like to reply to Mrs. Constance Lynn's letter (*Journal*, April 2, p. 851).

First, good and effective relaxation is, as much as anything, an attitude of mind, and is achieved not by "trying to relax," or by diligent practising of a set of exercises, but by learning to "let go" mentally and physically. For this reason I

should be most careful to avoid the word "exercise," with its associations of gymnastics and effort, in connexion with relaxation. Secondly, those who teach relaxation to expectant mothers should be very careful to make it quite clear that the aim is to minimize *pain* in childbirth, and not to give a completely effortless and carefree labour. Anyone who has tried it will probably agree that giving birth to a child is the hardest work that a woman is ever likely to do, and it is most important that she should realize this. Mrs. Lynn states that she herself was "totally unprepared for the really serious and hard business involved."

My own confinements were all normal and straightforward, and during each I was able to practise relaxation with excellent results. For the first I was Dr. Dick Read's patient, and had no anaesthetic or analgesic. The only really unpleasant part was at the end of the first stage, and during the birth of my second child the pain at this point was effectively relieved by pethidine.

During my third labour I was led by sheer curiosity to try the gas and air machine brought along by the midwife, but I most certainly would not use it again. In my opinion it leads to lack of co-ordination, with subsequent loss of control and ability to co-operate in the second stage. Most people with no personal experience of childbirth seem to think that some form of anaesthetic is necessary at the moment of crowning, but I have not found this to be painful, although naturally it is extremely uncomfortable. For a woman who is still alert and unfuddled this can be an exciting moment of approaching achievement, and it is so soon followed by the joy of hearing the child's first cry that it is well worth the discomfort.

It seems to me that in normal conditions, knowing how to relax and how to use that knowledge, with possibly some relief from pain when full dilatation is near, the average woman should be able to achieve and enjoy natural childbirth. That she does not do so in many cases leads one to suspect either that she has been taught wrongly or that she herself is, for one reason or another, incapable of relaxing properly. I feel that Mrs. Lynn is a little hard on a system which many people have found helpful, her only evidence being that it does not work for her personally.—I am, etc.,

London, N.10. ALISON DUDDINGTON.

SIR,—As one who has obviously followed the correspondence "Whither Natural Childbirth?" I feel justified in replying to Mrs. Constance Lynn's letter (*Journal*, April 2, p. 851) not only as a mother of two children—the first born after I was aged 30 by caesarean section and the second, a 9 lb. (4 kg.) boy, three and a half years later, absolutely naturally after a labour lasting less than four hours—but also as one who has taught some hundreds of women this approach to childbirth and been present at the labours of most of them. Therefore I write as a teacher with considerable labour ward experience, and as a mother.

With all due respect to this lady's ability, I cannot help feeling that in fairness to her instructress, and perhaps those who attended her confinement—before she states "categorically . . . "—a full description of her conduct during labour should be made clear to her readers. It seems strange to me that, if she had been taught this method in its entirety, she could have been "totally unprepared for the really serious and hard business involved." I find this difficult to understand if her antenatal teaching had been correctly carried out, for the woman, adequately instructed, is always told to expect "serious and hard work." After all, is this not the meaning of the word "labour"? I also find it difficult to understand her remark, "A great deal of what I was taught to do was physically impossible in labour, and much of what was possible, one hadn't the inclination to do at that time." It appears that Mrs. Lynn, once my husband's "most ardent and loudest fan," allowed her enthusiasm to override a practical and commonsense approach to a perfectly natural function—woman's most cherished heritage.—I am, etc.,

Petersfield. JESSICA DICK READ.

Purpuric Drug Eruption Caused by Carbromal

SIR,—Dr. Peter Borrie (*Journal*, March 12, p. 645) cites six cases of a purpuric eruption which he attributes to carbromal. During the course of my practice over a number of years I have prescribed carbromal in one of the forms mentioned—that is, "persomnia"—regularly to many patients, including many children, and never have I encountered, as a result, any skin eruption or, indeed, any other untoward side-effects.

In the article Dr. Borrie emphasizes that the dose of carbromal (which varied between 3 gr. (0.2 g.) and 20 gr. (1.3 g.) nightly) "bore no relationship to the severity of the eruption." This seems to be an indication that individual idiosyncrasy (allergy) was the possible causal factor involved, although my own experience tends to indicate that the incidence of such an idiosyncrasy, if present, is less than that which one commonly associates with penicillin or aspirin. In view, therefore, of the efficacy and enormous margin of safety of carbromal and other of the open-chain ureide series, compared with the barbiturates, the incidence of any such side-effects would appear to be almost clinically negligible. It is also worth noting that all the cases described apparently cleared up completely without treatment.—I am, etc.,

London, E.18. G. F. NEWBOLD.

Chronic Discoid Lupus Erythematosus

SIR,—I was very interested to read the article (*Journal*, February 5, p. 329) by Dr. H. J. Lewis on the treatment of chronic discoid lupus erythematosus with chloroquine sulphate. Since reporting a case so treated in 1953[1] I have had the opportunity of treating five more cases without a failure, and I can completely endorse Dr. Lewis's conclusion that chloroquine sulphate is as efficient a form of palliative therapy as any previously used. The average maintenance dose has been one tablet of chloroquine sulphate daily—equivalent to 150 mg. of base.

My original patient, who has been on therapy for almost two years, has continued to improve, although on one occasion when she stopped her treatment there was an almost immediate relapse.—I am, etc.,

Bulawayo, S. Rhodesia. J. CHARLES SHEE.

REFERENCE

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Swallowed Hair-grips

SIR,—In view of the recent correspondence on the above subject, may I submit details of an interesting and unusual case which came under my care whilst resident surgical officer at the Barnsley Beckett Hospital some years ago?

A single girl of 19 said she had swallowed a hair-grip several days previously. *X*-ray showed the presence of a hair-grip placed centrally in the lower hypogastric region, considered therefore to be in the lower coils of the ileum. She was asked to attend again in two days' time. Further *x*-ray then showed no appreciable change in the position of the hair-grip; she had no symptoms. A third *x*-ray two days later showed no change. She complained of suprapubic ache and discomfort, but there were no abnormal physical signs. She was admitted for observation. Next day she passed a small amount of blood in her urine. She was cystoscoped, and the hair-grip was seen in the bladder, covered with greyish-white phosphatic concretion, with a globular enlargement over the crook of the hair-grip, looking very much like a small doll. There was an associated cystitis. She readily gave written consent to operation and removal. I removed the foreign body by suprapubic cystotomy and noted that her uterus was enlarged to the size of approximately a 10- to 12-weeks gestation. She was discharged on the tenth day without complications.

It was difficult to determine when this hair-grip was inserted, although it was obvious that she had used it in

an attempt to induce abortion. She persistently maintained that she had swallowed the hair-grip, and denied vigorously that she was pregnant. I understand that subsequently she was delivered of a full-term infant.—I am, etc.,

Leeds. ISAAC ROSE.

Malignant Melanoma and Pregnancy

SIR,—We were interested in Dr. H. Stewart's report (*Journal*, March 12, p. 647) of a case of malignant melanoma in which neoplasia was stimulated during pregnancy, and his comment that this association has rarely been reported.

We have recently seen a case of malignant melanoma in a woman of 29. A pigmented naevus was removed from the patient's left leg in June, 1953, during her second pregnancy. The area was widely excised, when the section showed a malignant melanoma. Her child was safely delivered and she was well and showed no signs of recurrence until January, 1955, when a lump was first noted in the left groin. She was then in the 24th week of a further pregnancy. Excision proved this to be a secondary deposit from a malignant melanoma and she has now been evacuated to England for further treatment.—We are, etc.,

Benghazi. M. A. W. ROBERTS.
E. I. KOHORN.

Hypoglycaemia in Chronic Alcoholism

SIR,—Dr. J. S. Taylor (*Journal*, March 12, p. 648) described the interesting case in a chronic alcoholic of fatty liver changes producing hypoglycaemic attacks. Fatty liver is very common in chronic alcoholics, in whom its incidence has been estimated at 75%.[1] Of 150 alcoholics at Warlingham Park Hospital—the great majority of whom showed no liver enlargement—approximately 75% had abnormal results in at least one out of a number of liver function tests (carried out by Dr. W. W. Kay). Most frequently positive was the bromsulphalein test—that is, in approximately one-third of the 80 patients in whom it was performed.

As far as hypoglycaemia in alcoholism is concerned it has been pointed out that the symptoms of impending hypoglycaemic shock resemble alcoholic "jitters,"[2] and it has been suggested that hypoglycaemia may be responsible for neurotic symptoms occurring in chronic alcoholics.[2 3] Tintera and Lovell[4] suggest that, following primary and secondary hypofunction of the adrenal cortex in alcoholics, craving for alcohol results when blood sugar falls to a certain low level. Lovell[5] explains the alcoholic's apathy, physical weakness, etc., as being caused "to a large measure" by his low blood sugar (according to others[6] the chronic alcoholic's fatigability is "in great part . . . a consequence of protein, and particular vitamin, shortage"), and ascribes the "often astonishingly rapid" response of alcoholics to adrenal cortex extract to the restoration of the blood sugar balance and of liver functioning. The importance of the restoration of blood sugar balance in alcoholics has been stressed repeatedly,[2 3] and according to Lolli[7] "some cases of alcohol addiction are precipitated (but not caused) by an underlying spontaneous hypoglycaemia, correction of which is an adjuvant to treatment of the addiction."

An investigation in 21,000 non-alcoholics showed hypoglycaemia below 80 mg. in 11% of cases.[8] In alcoholics relatively low fasting blood sugars were frequently found by Strecker and Chambers[2]; Voegtlin *et al.*[9] found hypoglycaemia in 17.1% and hyperglycaemia in 6.6% of 303 chronic alcoholics, Feldman[10] saw among 150 alcoholics a level below 0.80 g./l. in 1.34%, between 0.80 and 1.10 g./l. in 95.33%, and between 1.11 and 1.20% g./l. in 3.33% (Hagedorn's method), and Valera *et al.*[11] found no difference between alcoholics and non-alcoholic controls. In our own material of 135 alcoholics the average blood sugar level for 102 males was 86 mg./100 ml., for 33 females 97 mg./100 ml., for the total of 135 89 mg./100 ml. (method modified after King). The level was—in mg./100 ml.—below 80 in 35%, between 80 and 120 in 61%, above 120 in 4%. According to King,[12] 80% of normal adults have a fasting blood sugar value between 68 and 96 mg./100 ml., 10% have a lower and 10% a higher level; the corresponding percentages among our alcoholics were 58, 14 (below 68 mg./100 ml.) and 28% (above 96 mg./100 ml.) respectively.

Results of glucose tolerance tests too show great differences. "Lower than average" curves "as a whole" were noted by Strecker and Chambers,[2] no difference in glucose tolerance between a group of male alcoholic addicts and a control group of male abstainers and social drinkers was observed by Varela *et al.*,[11] a decrease in glucose tolerance in 41% of 303 alcohol addicts was found by Voegtlin *et al.*,[9] an increase in tolerance in 44% of 50 alcohol addicts by Karlan and Cohn.[13]

The considerable variation in the findings of different observers seems to support the view of Varela *et al.*[11] that whilst "a sizable proportion of alcohol addicts exhibit a normal glucose tolerance," "the population of alcohol addicts is sufficiently irregular, in respect to glucose tolerance, to yield different results in different samples," thus reflecting also in this aspect the fact that alcoholics are not a homogeneous group of people.—I am, etc.,

Warlingham, Surrey. M. M. GLATT.

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Tetracycline

SIR,—In your annotation on tetracycline (*Journal*, April 2, p. 838) you mention a paper by Frei and his co-workers[1] in which they compared the use of penicillin and tetracycline in the treatment of pneumonia. Twenty-six patients were given tetracycline in what they state "a relatively high dosage of 4 grammes a day," and 31 patients were given a relatively small dosage of 600,000 units of aqueous potassium penicillin. What were they trying to find out? They had read that Finland[2 3] had demonstrated that with the use of chlortetracycline, oxytetracycline, and tetracycline the frequency of diarrhoea differed directly with the dosage. When tetracycline was used in a dosage of 1 to 1.5 g. daily, 2% of patients had diarrhoea. When the dosage was increased to 2 g. a day this percentage rose to 5, and they have now demonstrated that on 4 g. a day this side-effect occurred in 15% of patients. All the 31 patients in the penicillin group suffered no ill-effects. A similar study in the treatment of pneumonia was carried out by the Medical Research Council in 1951.[4] Patients in this study were given an initial dosage of 2 g. of aureomycin, and then 1 g. every six hours. As was to be expected with this dosage, side-reactions with aureomycin were much greater than with penicillin.

These two studies did not take into account the recommended dosage of aureomycin. This dosage was arrived at after consideration of extensive pharmacological investigations and the results of clinical studies undertaken throughout the world. In the large majority of cases the dosage of aureomycin and tetracycline should not exceed 1 g. a day for an adult. Each 250 mg. capsule should be given with a glass of cold milk or bland fluid. By this means side reactions may often be avoided.[5] Further comparative studies on how much more of the tetracyclines the patient can stand are, in my opinion, of little value. In the light of recent work on the effectiveness of small amounts of

antibiotics[6] surely it should be the aim of clinical investigators to determine the smallest amount of antibiotic that is effective therapeutically. It has been stated[6] that if the lowest effective dose of an antibiotic is used the infecting organism is unlikely to become resistant. Since the development of resistance to all the antibiotics is a subject of major clinical importance, and the excessive use of antibiotics appears to predispose to this development, it cannot be too strongly emphasized that practitioners should not use at the present time a dosage in excess of that recommended in the *British Pharmacopoeia* (1953). The publication of papers on ill effects produced by excessive dosage of antibiotics will have one good result if it focuses attention on the importance of correct dosage.

Your annotator also comments that if tetracycline produced fewer side-effects than either aureomycin or terramycin, the importance of this advantage should not be minimized. That terramycin produces fewer side-effects has been shown in at least six published papers in the last few months. In this country Abbott and Parry,[7] using a dosage of 1–2 g. daily of tetracycline, found no side-effects from its use. In a study of tetracycline Wilson[8] stated that "side-effects were uncommon and unimportant." In a comparison of 180 patients treated with the tetracyclines Weaver and McCorry[9] have noted that the incidence of side-effects with tetracycline was half that encountered with the use of oxytetracycline. The paper of Finland has already been referred to in which he noted that side-effects from tetracycline were minimal. The evidence available shows that tetracycline has certain unmistakable advantages over oxytetracycline and chlortetracycline which cannot be arbitrarily dismissed with the statement that the tetracyclines have the same toxicity.—I am, etc.,

A. T. MENNIE,
Medical Director,
Lederle Laboratories Division,
Cyanamid Products Limited.

London, W.C.2.

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Temporal Lobe Epilepsy and the Psychoses

SIR,—I was interested in the valuable paper on "Psychical Phenomena in Temporal Lobe Epilepsy and the Psychoses" by Drs. Shafica Karagulla and E. Elizabeth Robertson (*Journal*, March 26, p. 748), but I wonder how justified are their comparisons between the two diseases. Surely the analogous symptoms are produced by the fact that they are both the result of a disorganization of the same machine, but this does not imply that the nature of the disorganization is similar. To take a simplified example, a "knock" in an internal combustion engine can be produced by poor fuel, a wrongly timed ignition, or a worn big end. Yet no one suggests that the causation is similar.

Again, what of those psychoses which are produced rapidly in a few hours by great strain? Or in a case which I saw many years ago in which the psychosis disappeared almost instantly? This was that of a woman about 40 years of age who was suffering from a paranoid psychosis and a coincidental mitral stenosis. She was grossly hallucinated and deluded, and spent most of her time parading the ward shouting at those who seemed to be persecuting her. Suddenly in the midst of her shouting she developed an embolus in her left middle cerebral artery. She did not lose consciousness, but at once had a right-sided hemiparesis and complete aphasia. After many weeks her paralysis recovered and her speech came back. She was then able to tell me that the "voices" had ceased at once, at the very moment her limbs became paralysed and she lost her power to talk. Obviously, with the abolition of her power to express herself in words the internal ideational constructive power was abolished. This was the source of the hallucinations, and the "voices" ceased magically. Such an experience does much to uphold J. B. Watson's[1] view that thought is only suppressed speech. It suggests also that schizophrenia is a purely functional illness and that it is not caused by foci of deterioration such as one finds in epilepsy.—I am, etc.,

London, W.1. CLIFFORD ALLEN.

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Speaking Up

SIR,—The correspondence on poor standards of speech at medical meetings (*Journal*, April 2, p. 853) gives me the opportunity to comment without, I hope, appearing impertinent to my seniors. I submit that the pathetic and irritating mumbling usually inflicted on the audience at learned medical societies is due to the following factors: (1) nervousness, and the traditional Englishman's reluctance to make himself conspicuous; (2) the fear that emphatic oratory will be ridiculed as conceit or charlatanism; and (3) laziness; many eminent doctors do not seem to realize the importance of clear and emphatic public speaking, and would consider it beneath them to learn how to prepare and deliver an address.

Frequently the speaker resorts to reading (or mumbling) verbatim from a script. But why "read papers"? Matter designed to be assimilated by the eye is seldom ideally composed for absorption by the ear, even if clearly read. Medical papers should be printed in the appropriate journal or "proceedings" shortly before the meeting. The writer could then deliver (not read) a short summary, and the matter could then be discussed (surely the real value of such gatherings) before most of the audience had left to catch trains or sunk into coma.—I am, etc.,

London, W.1. NORMAN A. PUNT.

Night Cramps

SIR,—May I point out that your annotation on night cramps (*Journal*, March 12, p. 653) omitted to mention the value of nicotinic acid or nicotinamide in preventing such cramps? Nicotinic acid was recommended some years ago in answers to "Any Questions?"[1] and I have found it to be efficacious.—I am, etc.,

Chalfont St. Giles. H. H. KING.

REFERENCE

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Hysterical Hyperventilation with Carpopedal Spasm

SIR,—A girl of 8 years was seen recently who had developed a morbid fear of appendicitis. One of her schoolfriends had recently had her appendix removed, and, from personal knowledge of this latter child, I am sure that no morbid details were spared in conversation. The former child was the third in a family of four girls, and, unlike the others, seemed to be withdrawn and perhaps a little emotionally unstable.

The first episode occurred one evening when she cried out with sudden severe abdominal pain. The pain continued for half an hour and was alleged to be in the umbilical region. A full clinical examination failed to provide a diagnosis, and, as the pulse rate and temperature were normal and the pain had mysteriously passed away, the child was reassured and was soon playing quietly. A visit several hours later revealed no further developments. The second episode occurred 24 hours later. This time there were pains in the abdomen, a choking sensation, and painful, paralysed arms and legs, with tingling. The child was sobbing uncontrollably and was hyperventilating for about 20 minutes. The hands were typical "*les mains d'accoucheur*." The child was reassured and a minute or so of breath-

holding stopped the painful spasm, and within five minutes the adducted thumbs relaxed. Shortly afterwards the choking sensation (due to a lump, presumably "globus hystericus") disappeared and a full clinical examination revealed nothing to suggest appendicitis.

The mother admitted that the child had a dread of developing appendicitis. This started about the time the schoolfriend returned from hospital with an account of her experiences.—I am, etc.,

B.A.O.R., 33. J. CLARKE.

Acute Respiratory Obstruction

SIR,—I have read with great interest Mr. Norman Jory's article on acute respiratory obstruction (*Journal*, March 26, p. 781). In the paragraph on laryngoscopy he states that if the mouth cannot be opened because of spasm this may be overcome by the intravenous injection of 50 mg. of suxamethonium chloride. This is undoubtedly most effective. However, I feel that it should be emphasized that not only will this relax the jaw muscles but that it will also relax the glottis and paralyse some, if not all, of the muscles of respiration, depending on the size of the patient, for a period of from three to five minutes. One will probably then be dealing with an apnoeic patient; certainly there will be no deep breath.

I suggest, therefore, that if this line of treatment be carried out it should be stressed that one must be prepared to apply adequate artificial respiration, preferably with oxygen, until such time as the effect of the relaxant has ceased.—I am, etc.,

Blackrock, Co. Dublin. K. P. O'SULLIVAN.

Selection of Patients for Psychotherapy

SIR,—Dr. E. A. Bennet's lecture at the St. Marylebone Hospital for Psychiatry and Child Guidance, as summarized in the *Journal* (April 2, p. 844), comprises the broad wisdom which is linked with his name. The address, as such, would most certainly have met the wishes of his audience; he could, however, have delivered it with equal facility 30 years ago.

It is a sombre reflection, if valid, that advice on psychotherapeutic procedure remains a personal rather than a clinical issue. It is a distressing thought, if true, that the word depressive is used to denote the indication for either electric convulsion therapy or psychological interference. It is a disconcerting cogitation that the diagnosis of obsessional neurosis, as described by Freud during his formative years in Vienna, bears little resemblance to the nowadays use of the term obsessional. The latter depicts a psychiatric state which, dependent on the predilection of the physician consulted, may be treated either by prefrontal leucotomy or one or other of the disparate psychotherapeutic techniques.

The inference seems to be that competent selection of patients for psychotherapy demands a strict application of intelligence of the head rather than what Dr. Bennet calls an "intelligence of the heart."—I am, etc.,

London, W.1. MURDO MACKENZIE.

Investigations on Everest

SIR,—With reference to the paper on "Some Effects of High-altitude Climbing," by Dr. D. Stafford Matthews *et al.* (*Journal*, March 26, p. 768), it is stated that the authors have not seen the results of any investigations conducted on Everest. I append a list of references[1–8] to work done on Everest which has already been published. Further results will appear shortly.—I am, etc.,

London, N.W.3. G. PUGH.

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Obituary

A. F. MacCALLAN, C.B.E., M.D., F.R.C.S

Mr. A. F. MacCallan, consulting ophthalmic surgeon to the Westminster Hospital and the Royal Eye Hospital, and pioneer in the study and eradication of trachoma; died in Westminster Hospital on March 31 after a short illness. He was 83 years of age, and had continued in active practice until a few weeks before his death.

Arthur Ferguson MacCallan was born on October 23, 1872, the only son of the Rev. J. Ferguson MacCallan, vicar of New Basford, Notts. He was educated at Charterhouse, Christ's College, Cambridge, and St. Mary's Hospital Medical School, where he was a university exhibitioner. After qualifying in 1898 he graduated M.B., B.Ch. in the following year and also took the F.R.C.S. He completed his ophthalmic training by three years as house-surgeon at Moorfields Eye Hospital, and almost immediately afterwards (1903) was appointed as ophthalmologist in the department of public health, Cairo. Here he remained for 20 years, interrupted only by his service in the R.A.M.C. during the first world war, when he was mentioned in dispatches.

It was while MacCallan was in Egypt that Sir Ernest Cassel, having successfully financed the building of the Great Aswan dam, had decided to confront the vast problem of trachoma, which had been a scourge of Middle East countries since prehistory, by the training of a corps of Egyptian oculists. To this end a travelling eye hospital was formed which offered scope for all the energy, enterprise, and administrative ability that MacCallan so happily embodied. His success was immediate, and eye hospitals were built in all the major provinces staffed by his enthusiastic pupils. By the time he returned to England mass treatment had been instituted, and the disease seemed to be at least under some sort of control. He retired with the honours that he deserved, receiving for his ophthalmic services to the Egyptian Government the Order of the Nile (second class) and the Order of Medjidieh (third class), and being appointed C.B.E. in 1920 and an officer of the Order of St. John of Jerusalem. His work was commemorated in 1931 when a bronze bust, commissioned by the ophthalmic surgeons of Egypt, was unveiled by the British High Commissioner. His major textbook on trachoma, published in 1936 and translated into many languages, remained for many years an authoritative guide.

MacCallan returned to England in 1924 and started a practice in London. In the same year he saw an advertisement in *The Times* for the post of assistant ophthalmic surgeon to Westminster Hospital, and he successfully applied for this. He was later appointed also as surgeon to the Royal Eye Hospital. On reaching the age of 65 in 1937 he retired from the active staff of the Westminster, but he returned to the hospital during the second world war, when the ophthalmic department had been depleted of consultant staff on the death of Mr. A. D. Griffiths. Thereafter he still continued his researches in trachoma in a laboratory at the Westminster Medical School. In 1935 he was appointed as second president of the International Organization against Trachoma, a high office that he held for 20 years until, at the International Congress of Ophthalmology in Montreal last autumn, he handed over the

active leadership to Dr. G. B. Bietti, but was himself appointed honorary life president in recognition of his great and long services: by the same token he was also appointed a life member of the Ophthalmological Society of the United Kingdom, of which he had been vice-president. He had also served as secretary and vice-president of the Ophthalmological Section of the Royal Society of Medicine, and was a distinguished member of many foreign ophthalmological societies. In 1918 he married Hester, daughter of the late Bishop Boyd Carpenter, and she survives him, together with two sons and a daughter.

P. D. T.-R. writes: A. F. MacCallan was an unforgettable personality. From his early days in the mid-Victorian vicarage, through a long and inspiring term of office in Egypt, at his English hospitals, and finally as chairman of his own parish council in Hertfordshire, his life was coloured by a sense of duty and dedication that fully merited the renown he won. Forthright and vigorous, intolerant of obstruction, he was ideally suited to driving through the inertia that has blocked progress in the Egyptian health services for so many years. Yet his dynamic mien was at all times leavened by especial charm of manner and a readiness of humour that stole the affection even of his critics. He belonged to a vanished generation of empire builders, and his war against the trachoma virus was on a heroic scale; while the gratitude of countless near-blind is his just reward.

G. F. PETRIE, M.D.

Dr. George Petrie, who was for many years on the staff of the Lister Institute of Preventive Medicine and finally retired in 1944, died on March 17, aged 81.

After a short period as a student at Edinburgh University George Ford Petrie continued his medical education at Aberdeen, where he graduated M.B., Ch.B. in 1898; five years later he proceeded to the M.D. with highest honours. It was while he was a student that he developed a keen interest in pathology and bacteriology, and after a short period as an assistant in general practice in Yorkshire and as a research student in the Lister Institute he was appointed assistant bacteriologist to the Institute in 1902, working in the serum department at Elstree under the late Dr. George Dean. From then on he took an increasingly important part in many of the investigations designed to throw light on the aetiology and control of epidemic diseases. In 1905 he was a member of the Indian Plague Commission under the late Sir Charles Martin, and from 1911 to 1913 was bacteriologist under Dr. Charles Todd to the Plague Investigation Commission set up by the Egyptian Public Health Department. He also went with the British Delegation to the International Plague Conference in China in 1911, contributing a review of an outbreak of plague in North China to the published proceedings of the conference. About this time he was the author of several other articles on the subject of plague, including a report on the examination of rats collected in Suffolk and Essex. After serving in the R.A.M.C. as a bacteriologist in France during the first world war, he returned in 1919 to the serum department of the Lister Institute, succeeding Dr. MacConkey as bacteriologist in charge in 1926. He became a leading authority on antisera, particularly in connexion with their production in quantity, and it was largely due to his work that it was possible to produce quickly the large amounts of tetanus antitoxin required for the civil population in the last war. He should have retired in 1939, but after a very brief period of rest he returned to work in October, 1940, first to take charge of the library of the Lister Institute, then temporarily housed in Aldenham School, and in 1941 he again took over the supervision of the serum department during the absence of Dr. C. R. Amies in the R.A.M.C.

Dr. Petrie was the author of many papers on subjects connected with his specialty, and in 1934 he collaborated with the late Sir Alexander Fleming in writing *Recent Advances in Vaccine and Serum Therapy*. After he had retired he compiled an anthology of *British Medical Science and Practice*, and he was engaged on other literary work at the time of his last illness.

O. D. BROWNFIELD, C.B., O.B.E., M.B.

Surgeon Rear-Admiral O. D. Brownfield, who served in the Royal Navy for nearly 36 years, died on March 29 aged 64.

Owen Deane Brownfield was born on February 22, 1891, the son of Dr. H. M. Brownfield, of Petersfield. From Epsom College he went on to St. Thomas's Hospital, qualifying in 1914. He entered the Royal Navy as a temporary surgeon-lieutenant in October of that year, and during the first world war he served at the R.N. Hospital, Haslar, and in H.M.S. *Excellent*, H.M.S. *Chester*, and at the R.N. Barracks at Portsmouth. In 1919 he was awarded the O.B.E. for valuable services given while serving in these appointments. Having graduated M.B., B.S., London, after the war he was transferred to the permanent list of the Royal Navy towards the end of 1919, and promoted surgeon lieutenant-commander. From 1931 to 1935 he was medical specialist at the R.N. Hospital, Malta, holding the rank of surgeon-commander, and then after a period at sea he was placed in charge of the cadets' sick quarters at the R.N. College, Dartmouth, in 1937. In 1940 he was appointed to H.M. Hospital Ship *Vita* as medical officer in charge and holding acting rank as surgeon-captain. He was confirmed in this rank in 1941. After a period of service at the R.N. Auxiliary Hospital, Barrow, Burney, he became medical officer in charge at the R.N. Auxiliary Hospital, Trincomalee, Ceylon. On his return to the United Kingdom in 1945 he was principal medical officer at H.M.S. *Collingwood* until 1947, when he was promoted surgeon rear-admiral. Until his retirement in 1950 he was medical officer in charge at the R.N. Hospital, Malta. Surgeon Rear-Admiral Brownfield was appointed C.B. in 1948, and for three years before he retired he was King's Honorary Physician.

After his retirement he returned to live in Petersfield and became a member of the Council of the B.M.A. in 1951. He was also a member until the time of his death of the Armed Forces Committee and the Waverley Evidence Committee, playing a full part in the deliberations of these committees. His many old friends in the Navy and the new friends he made as a result of his interest in the work of the B.M.A. will regret the passing at a comparatively early age of one who served his country and his profession so faithfully and so well.

E. C. SPRAWSON, *M.C.*, D.Sc., F.D.S. R.C.S. M.R.C.S.

The sudden death of Professor Evelyn Sprawson, which took place at a committee meeting in London on April 6, removes a considerable figure from the field of dental surgery and research. He had held the chair of dental surgery and pathology of the University of London, and was consulting dental surgeon to the London Hospital, where he had formerly been director of dental studies.

Evelyn Charles Sprawson was born on February 18, 1881. From King's College School, London, he went on to study dentistry at the Royal Dental Hospital, where he won the Walker and Saunders scholarships. After a further period of study at Charing Cross Hospital he qualified in medicine in 1905, winning medals for ophthalmology and midwifery, and shortly afterwards he joined the staff of the dental school at the London Hospital, where in the course of his career he achieved great distinction not only as a practising dental surgeon and as a teacher but also as a wise adviser in the affairs of his profession. He served on numerous Government committees and as one of this country's representatives at international congresses all over the world. An obituary column could readily be filled with the titles of the various offices he held during his career. He had been deputy chairman of the Dental Advisory Council; chairman of the Board of Studies in Dentistry and member of the Faculty of Medicine of the University of London; and examiner in dental surgery to the Royal College of Surgeons, to several universities (including two overseas), and the Dental Board of the United Kingdom. He served on the Medical Research Council committee for the investigation of the causes of dental diseases, and was a member of the Home Office Tribunal for the Dangerous Drugs Acts. The reputation he had gained as an investigator was shown by his election to the presidency of the International Association for Dental Research and to the honorary presidency of the Section of Histology when the International Dental Congress met in Paris in 1931. The year 1940 saw his election to the presidency of the Odontological Section of the Royal Society of Medicine, in which he was for many years a frequent contributor to the discussions. He had also been president of the Dental Officers Group of the Society of Medical Officers of Health. Sprawson, who held the degree D.Sc. of London University, was elected F.D.S. R.C.S. in 1947. Ten years earlier he had been Hunterian Professor at the College, and he was the Sir John Tomes prizeman in 1930.

In all that concerned the welfare of his profession Sprawson took an eager interest. His work on the council and committees—often very detailed and anxious work—of the Medical Protection Society occupied much of his time. He had been a member of the British Medical Association for 45 years.

Many papers by Sprawson appeared in the proceedings of scientific bodies concerned with dentistry and allied subjects, and he collaborated in the editorship of the last four editions of *Dental Surgery and Pathology*, the work so closely associated with his old colleague and chief, Sir Frank Colyer. He was also editor of the *British Dental Annual*. In the first world war Sprawson served with the R.A.M.C. in the British Expeditionary Force and was mentioned in dispatches and awarded the Military Cross. For many years he was a member of the 28th Battalion of the County of London Artists Rifles and received the Territorial Forces efficiency medal. In the last war he was consulting dental surgeon in certain of the sectors of the Emergency Medical Service. His chief interest outside his profession was aviculture, which he followed at his Surrey home and on which he wrote occasional papers.

We are indebted to Mr. A. M. A. MOORE for the following appreciation: By the sudden and unexpected passing of Professor Evelyn Sprawson, England has lost one of her most distinguished dental surgeons. He was an eminent contributor to our knowledge of many of the problems of dental surgery, and very many members of the dental profession in practice to-day owe much to his teaching and inspiration.

Sprawson was a shy, quiet, and retiring man, who took the greatest personal interest in the students working in his department, and he will always be remembered for his many kindnesses and acts of generosity to those in need. For many years he held the post of honorary consultant dental surgeon to Dr. Barnardo's Homes, and continued to attend the children at the homes long after his retirement from the staff of the London Hospital. It gave him great joy to feel that he was helping in some way to carry on the work of the founder, and it was a constant pleasure for the members of the staff to meet and work with this remarkable man.

Sprawson had much to do with the original establishment of the dental department at the London Hospital, which has now grown into one of the larger teaching units of dental surgery in the University of London. He played an active part in the life of the university and was one of the few dental professors to be granted the degree of doctor of science. Before his retirement from the staff of the London Hospital some years ago he was presented with his portrait by past and present members of the dental school—the only dental surgeon of the London Hospital to be honoured in this way so far. This portrait now hangs in the students' dining room of the London Hospital Medical College, and will be a constant reminder to future generations of a very great man.

Medico-Legal

MISTAKE NOT NEGLIGENT

A young, newly qualified hospital doctor, in discharging a man who went out into the street and collapsed and died of coronary thrombosis, made a mistake but was not negligent, said Mr. Justice Ashworth at Liverpool Assizes on April 1. He was giving judgment for the West Cumberland Hospital Management Committee and Dr. J. P. Graham in an action for damages brought against them by Mrs. Elsie A. Parkinson, of New Brighton, Cheshire. Her husband, Mr. S. A. E. Parkinson, aged 39, a crane driver, was found dead near Workington Infirmary on July 11, 1953.

In his judgment Mr. Justice Ashworth said that Parkinson went to the infirmary soon after 4 a.m. on the day he died and complained of chest pains. Dr. Graham, then house-physician there, gave him two tablets of codeine and told him to return later for *x*-ray examination. A quarter of an hour afterwards Parkinson was found dead near the hospital, and the judge said he was satisfied he died from a massive coronary thrombosis. The fact that Dr. Graham took an hour over the examination showed he was anxious on this, his fourth day at Workington, to acquit himself well, and the judge accepted his account of what he saw and did. It was conceded that the diagnosis was mistaken.

After hearing medical witnesses the judge said he had come to the conclusion that Dr. Graham was not negligent in failing to diagnose coronary thrombosis, and was not negligent in rejecting coronary thrombosis. If that was so, he was not negligent in sending Parkinson home, and there was not a sufficient element of uncertainty in his mind to require him to send for his superior. He made a mistake, but was not negligent. The judge said that even if the plaintiff had succeeded the damages would have been very small. Even if rest or treatment might have prolonged Parkinson's life, his future contribution as a breadwinner would have been negligible.

Dismissing the claim, the judge said: "I would like to add that if one merely knows that a man has died in the street in the early hours of the morning, after being discharged from a hospital to which he went in pain, one is

inevitably tempted to draw the conclusion that it ought not to have happened. That illustrates the danger of only knowing part of the story. Once one adds that in the hospital he was examined carefully for nearly an hour, and that the signs and symptoms on balance negatived any serious condition, then that first conclusion must in fairness be disregarded."

The defendants did not ask for costs.

The Medical Defence Union instructed Messrs. Hempsons, solicitors, to act for Dr. Graham.

ULNAR NERVE PARALYSED

An agreed settlement has been reached in an action for negligence brought at Leeds Assizes against two doctors and members of the nursing staff of Castleford, Normanton and District Hospital. The allegations against one doctor and against the nursing staff were withdrawn. The action was brought by Robert Bucktrout, aged 50, of Castleford, who claimed damages for personal injuries from the Leeds Regional Hospital Board and also from Dr. Elva M. Chivers, an anaesthetist, of Pontefract, and Dr. N. I. A. Shohet, then resident surgical officer at the hospital.

Bucktrout's case was that he was admitted to hospital on November 28, 1951, for operative treatment of perforated peptic ulcer. A male nurse, Mr. F. Calvert, first gave him an injection, and then in the operating theatre he was given an injection by Dr. Chivers in his left arm. The latter injection, he said, caused him pain before he became unconscious. Dr. Shohet performed the operation. When Bucktrout recovered consciousness he saw that his left arm had been tightly bandaged between the shoulder and elbow, and when the bandage was removed he saw the arm was black and swollen. The sequel to the operation was that the ulnar nerve was paralysed and Bucktrout was under hospital treatment until January, 1953.

When the hearing had been proceeding for five days a consultation between the parties resulted in their coming to terms on the basis that judgment should be given to the plaintiff with costs for £350 against the hospital board and against Dr. Chivers. As to Dr. Shohet, he was exonerated from any charge of negligence, and judgment was given for him against the plaintiff. Dr. Shohet did not press for costs. The hospital board and the doctors agreed to the settlement on the understanding that the plaintiff withdrew all allegations not only against the hospital board and the two doctors but also against the nursing staff of the hospital, and particularly against Mr. Calvert. The £350 damages were apportioned between the hospital board and Dr. Chivers.

Mr. Justice Slade said he thought the parties had been well advised, and he regarded it as a satisfactory settlement.

The Medical Protection Society instructed Messrs. Le Brasseur and Oakley, solicitors, to act for Drs. Chivers and Shohet.

Medical Notes in Parliament

Group Practice Loans

Miss PAT HORNSBY-SMITH, Parliamentary Secretary, Ministry of Health, told Mr. J. K. VAUGHAN-MORGAN (Reigate, Con.) on April 4 that at the end of March, 1955, some £36,000 had been paid to 11 partnerships in England and Wales, including 38 doctors, as loans for the establishment or improvement of group practice.

Inspection of Doctors' Surgeries

Mr. VAUGHAN-MORGAN asked when the current inspection of doctors' surgeries was expected to be completed. Miss HORNSBY-SMITH stated that inspections were being carried out under arrangements made by the British Medical Association and were, she understood, progressing well; but the Association could not yet say when they would be completed.

Poliomyelitis Research

Mr. GEORGE DARLING (Sheffield, Hillsborough, Lab.) asked the Parliamentary Secretary to the Ministry of Works, as representing the Lord President of the Council, whether he was satisfied with the scope of the research being undertaken to discover an anti-poliomyelitis vaccine, in view of the recent report of the World Health Organization, which showed that the incidence of poliomyelitis increased with improvements in living standards, that current methods of treatment had proved to be inconclusive, and that all hopes of dealing successfully with the disease depended on the discovery of a suitable vaccine. Mr. J. R. BEVINS, replying on April 4, said that an extensive programme of research on poliomyelitis vaccines was being supported by the Medical Research Council, by the National Fund for Poliomyelitis Research, and by certain pharmaceutical firms. The effort in this country was being co-ordinated by the Medical Research Council, and he was advised that all promising lines were being developed.

Colouring Matter in Food

Dr. A. D. D. BROUGHTON (Batley and Morley, Lab.) asked the Minister of Food what comments he had now received from the catering industry, from manufacturers of colouring materials used in food, or from other interested bodies on the report of the preservatives subcommittee of the Food Standards Committee concerning the preparation of an approved list of substances which might be added to food. Mr. HEATHCOAT AMORY stated on April 4 that the comments received to date related for the most part to points of detail concerning the recommended colours. Some objections had also been lodged against the principle of a restricted list of colours for use in food. Replying further to Mr. N. DODDS (Dartford, Lab.), he said that a period had been allowed for anyone who desired to do so to make representations. That period—to March 31—was now over, and he was actively considering what action was required. Dr. BROUGHTON asked the Minister to regard the matter as one of urgency in view of statements made in the report, and to make sure that coal-tar derivatives used in colouring food should be prohibited in the near future. Mr. AMORY assured him that there would be no avoidable delay in taking action.

Mr. DODDS asked the Minister of Food if he would ban the colouring of kippers with coal-tar dyes, and encourage a return to the practice of producing the appetizing appearance and health-giving properties by smoking instead of painting. Mr. AMORY replied that the addition to food of colouring matters including coal-tar dyes had been the subject of a recently published report by the Food Standards Committee. Consideration was being given to representations from interested parties with a view to a decision on the committee's recommendations. Mr. DODDS asked if the Minister could give a categorical denial that the dyeing of kippers was harmful to health. Mr. AMORY explained that his intervention must be limited to harmful effects. He was anxious to consider the recommendations and the representations made in connexion with these before he reached a decision.

Edinburgh Doctors' Survey

Mr. E. G. WILLIS (Edinburgh, East, Lab.) asked the Minister of Pensions and National Insurance if he was aware that in a recent survey made by 159 doctors of 5,086 elderly persons in Edinburgh it was found that over 200 were in need of financial assistance; and whether he would take steps to meet this hardship. Mr. MARPLES, the Parliamentary Secretary, replied on April 4 that he had seen an account of this summary in the Press, but he did not know on what basis the statements about financial need had been made. It was open to anyone in need to apply to the National Assistance Board.

Mr. WILLIS asked the Secretary of State for Scotland the following day if he was aware that in this survey it was discovered that there was a large need for physiotherapy;

and that of these elderly patients some 1,274 had need of domestic medical assistance and 1,270 were in need of nursing, hospital treatment, or rehabilitation; and whether he would take steps to deal with this. Commander GALBRAITH, the Under Secretary, replied that this survey was conducted as part of a joint study, in which Edinburgh Corporation and the South-eastern Regional Hospital Board were participating, of the needs of elderly patients in Edinburgh. The assessment of its findings, in particular as to the relative importance of the various needs reported by the general practitioners, was a matter primarily for these authorities, who would take careful note of them in considering the development of the various services for which they were responsible under Statute. Mr. WILLIS commented that the results of the survey should completely destroy the complacency of the Government about the conditions of old folk. Commander GALBRAITH retorted that there was no complacency. These particulars were collected so that a study could be made, and that was going on.

Army Medical Practice

Mr. S. HASTINGS (Barking, Lab.) on April 5 asked the Secretary of State for War what administrative arrangements were made to ensure that in peacetime a soldier who felt unwell could, as a right, claim to be seen by a doctor. Mr. ANTHONY HEAD told him that there was normally a daily sick parade at a fixed time attended by a doctor. A soldier who needed urgent medical attention would be seen either by the regimental medical officer or else, if special circumstances demanded, by a civilian doctor. He assured Mr. Hastings that the War Office aim was that in all cases decision whether a soldier should be seen by a doctor or not should not be taken by a person without medical training.

Mr. F. GOUGH (Horsham, Con.) asked when, and why, Royal Army Medical Corps surgical teams were removed from the establishment of a parachute battalion. Mr. HEAD stated that field surgical teams manned by the Royal Army Medical Corps had never been included in the establishment of a parachute battalion. They were held as an Army pool, and six were allotted to the Airborne Division. In airborne operations they dropped with the field ambulances providing medical aid. Mr. GOUGH said that during the war there were surgical teams with the battalions, who dropped with the battalions, and who saved thousands of lives. Mr. HEAD agreed, but said they were still held in a pool and attached to the battalions for operations, possibly for a prolonged period.

Hydrocortisone Ointment

Mr. A. R. W. LOW, Minister of State, Board of Trade, told Mrs. L. JEGER (Holborn and St. Pancras, South, Lab.) on April 5 that there were 91 licences issued in respect of hydrocortisone acetate ointment, to a value of £321, since January 1. Mrs. JEGER said the ointment was manufactured near Folkestone. It was only because of the unhelpful attitude of the Minister of Health that doctors outside the hospital service could only get the ointment by reimporting it. This was a waste of everybody's time. Would Mr. Low have a word with the Minister of Health and see if things could be improved? Mr. LOW replied that Mrs. Jeger would not like to deprive the people who were allowed to import the ointment of the right to do so.

Hospital Pharmacists

Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.) asked the Minister of Health whether he was aware of the shortage of pharmacists in the hospital service; and for how many assistants and senior assistants there were vacancies at the nearest available date. Mr. MACLEOD stated on April 4 that in August last there were deficiencies on complements of 281 in the basic grade and 64 in the senior grade. Dr. STROSS asked what the Minister had in mind to remedy the deficiency. Mr. MACLEOD answered, "Nothing very much at the moment." The main and obvious question was about salaries, and that was a matter for the Whitley Council.

Recruits to Dentistry

The MINISTER OF HEALTH announced on April 1 the following members of the Interdepartmental Committee which the Secretary of State for Scotland and he are setting up to inquire into the shortage of recruits to the dental profession: Sir Arnold McNair, Q.C. (chairman), Mr. J. E. H. Duckworth, L.D.S., Dr. J. L. Trainer, L.D.S, Dr. R. O. Walker, L.D.S., Sir Wilfred Fish, F.D.S., Professor F. C. Wilkinson, F.D.S., Mr. G. E. Gittins, M.A., Mr. I. D. McIntosh, M.A., Mr. G. R. Moxon, Mrs. Mary Stocks, B.Sc., and Professor A. P. Thomson, F.R.C.P.

Atmospheric Radioactivity

Mr. J. R. BEVINS, Parliamentary Secretary to the Ministry of Works, informed Dr. BARNET STROSS (Stoke-on-Trent, Central, Lab.) on April 6 that no measurements of atmospheric radioactivity in London earlier than 1947 were known. Since that date measurements of radiation backgrounds had been made in the physics department of the Royal Marsden Hospital; these were the measurements made under the auspices of the Medical Research Council. Other measurements made there since 1930 were designed to ascertain the degree of exposure of workers using *x*-ray apparatus and radium.

Mr. SOMERVILLE HASTINGS (Barking, Lab.) asked if the Government would initiate an inquiry into the genetic effects of radioactivity on human beings by means of an investigation of the biological history of those who were engaged in *x*-ray work some 40 or more years ago. Mr. BEVINS said that it was thought wise to await the report which the Government had invited the Medical Research Council to make. The Council's attention had, however, been drawn to Mr. Hastings's suggestion.

He added in a reply to Mr. ROY MASON (Barnsley, Lab.) that measurements of the radioactivity in the atmosphere at various heights showed that no danger had existed over these islands from thermonuclear explosions.

Fluoride Content in Water

Mr. J. GRIMOND (Orkney and Shetland, Lib.) on April 6 asked the Minister of Housing and Local Government what steps his department had taken under Section 111 of the Public Health Act, 1936, to check that water did not contain a degree of fluorine which rendered it unwholesome. Mr. D. SANDYS told him that the section mentioned required local authorities to satisfy themselves that the water supplies in their districts were wholesome. The advice of his medical and technical officers was available to them. Before he approved the use of a new public source he had to be satisfied that the proposed supply was wholesome, and in recent years particular attention had been paid to fluoride. His officers were collecting information about the fluoride content of the water supplied by statutory water undertakers in England and Wales, beginning with those serving a population of more than 100,000.

Claims for War Disability

Brigadier J. G. SMYTH told Mr. F. H. HAYMAN (Falmouth and Camborne, Lab.) on April 5 that the numbers of applications for war disability pensions referred to independent medical experts in each of the past three years, and the numbers in which advice favourable to the applicants was given, were: 1952, 49 and 10; 1953, 21 and 8; 1954, 18 and 3.

He gave Mr. Hayman the following totals of war disability claims and their result:

Year	Received	Accepted	Rejected
1952	27,850 (1,040)	11,940 (85)	13,060 (810)
1953	27,100 (1,260)	11,710 (105)	13,900 (740)
1954	23,200 (910)	9,600 (120)	12,550 (640)

The figures in parentheses relate to the 1914 war and are included in the main figures.

As a number of the claims accepted or rejected in each of the years 1952–4 were made in previous years, the sets of figures are not strictly comparable.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **March 26** (No. 12) and corresponding week 1954.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1955 Eng. & Wales	1955 Lond.	1955 Scot.	1955 N. Ire.	1955 Eire	1954 Eng. & Wales	1954 Lond.	1954 Scot.	1954 N. Ire.	1954 Eire
Diphtheria	11	0	3	0	2	14	0	9	1	0
Dysentery	1,815	204	334	18	1	1,315	194	366	2	23
Encephalitis, acute	4	0		0		6	3			0
Enteric fever:										
Typhoid	2	0	0	0	1	2	0	0	1	
Paratyphoid	4	1	1	0		20	0	0	1	
Food-poisoning	118	23				130	17		0	
Infective enteritis or diarrhoea under 2 years				12	12				14	11
Measles*	28,682	3337	435	605	116	2,067	32	176	32	452
Meningococcal infection	41	3	18	3	2	35	4	17	4	
Ophthalmia neonatorum	45	2	7	0		34	3	11	0	
Pneumonia†	984	46	257	11	42	661	41	222	12	9
Poliomyelitis, acute:										
Paralytic	6	1	0	1	2	15	1	4	0	
Non-paralytic	4	1				9	0			
Puerperal fever§	247	38	9	0		233	43	3	1	
Scarlet fever	815	35	102	50	18	1,492	94	166	38	35
Tuberculosis:										
Respiratory	646	65	132	21		785	92	147	29	
Non-respiratory	86	9	28	2		95	5	21	5	
Whooping-cough	1,867	128	137	50	63	2,553	93	466	30	58

DEATHS in Great Towns	1955 Eng. & Wales	1955 Lond.	1955 Scot.	1955 N. Ire.	1955 Eire	1954 Eng. & Wales	1954 Lond.	1954 Scot.	1954 N. Ire.	1954 Eire
Diphtheria	0	0	0	0	0	0	0	0	0	1
Dysentery	1	0	1	0		0	0		0	
Encephalitis, acute		0			0			0		0
Enteric fever	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	6	1	4	0	1	8	0	3	0	4
Influenza	48	8	0	0	14	22	3	1	0	0
Measles		1	0	0	0			0	0	2
Meningococcal infection		0	1				0	0		
Pneumonia	438	70	33	14	20	257	35	27	7	7
Poliomyelitis, acute	1	0			0	1	0			0
Scarlet fever		0	0	0	0			0	0	0
Tuberculosis:										
Respiratory	108	7	14	0	8	96	14	16	4	12
Non-respiratory		1	1	0	0			3	0	2
Whooping-cough	2	1	0	0	0	2	0	0	0	0
Deaths 0–1 year	245	29	38	6	11	270	30	30	9	14
Deaths (excluding stillbirths)	7,386	1070	760	163	282	5,906	836	706	128	188
LIVE BIRTHS	7,864	1194	961	232	508	8,346	1233	931	257	378
STILLBIRTHS	203	22	28			210	22	21		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Vital Statistics

Tuberculosis and Cancer in 1954

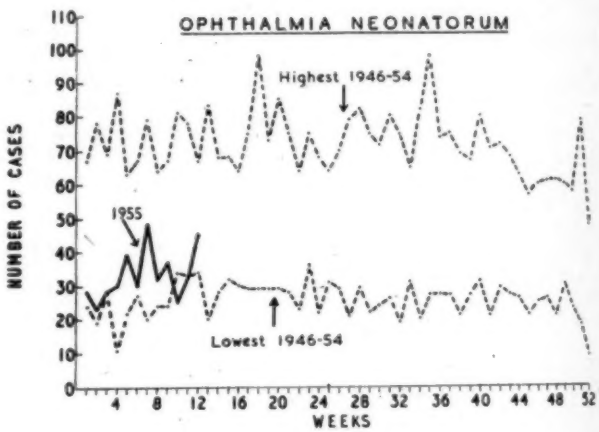
The total number of deaths in England and Wales from respiratory tuberculosis in 1954 was 7,069 (against 7,913 in the previous year), giving a provisional death rate of 160 per million persons. This is a decrease of 11% compared with the previous year, and means that since 1947 the death rate has fallen by more than 65%. The death rate from other forms of tuberculosis was 19 per million persons, compared with 22 for 1953.

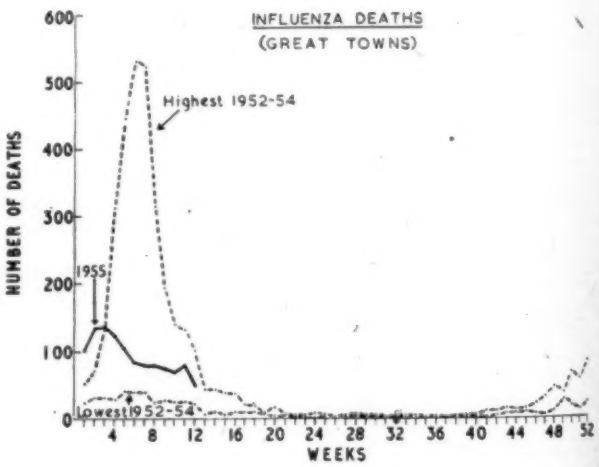
The provisional death rate for all forms of cancer for men was 2,222 per million population, and for women 1,862 : the 1953 figures were 2,165 and 1,835, respectively.

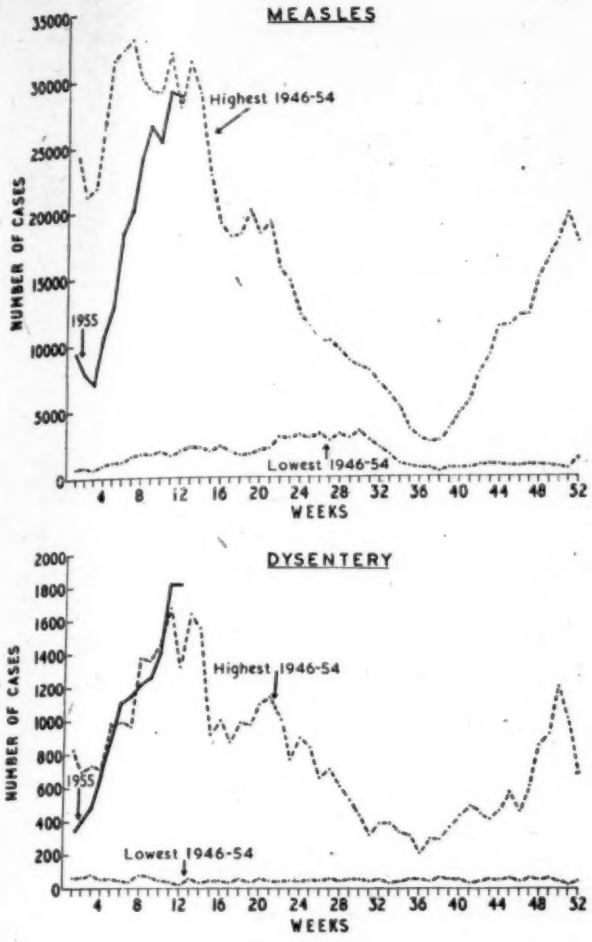
The rise in the rate for men includes an increase from 607 to 657 per million population for deaths assigned to cancer of the lung and bronchus, making a total increase since 1947 of 70%. The rate for cancer of the lung and bronchus for women increased from 98 per million in 1953 to 102 in 1954. Of the male deaths from cancer (47,319), 30% were certified as due to cancer of the lung and bronchus. Of the deaths of women (42,780), only 5% were so certified.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases (deaths for influenza) of certain diseases notified weekly in England and Wales (great towns for influenza). Highest and lowest figures reported in each week during the nine years 1946–54 (influenza, 1952–4) are shown thus ------, the figures for 1955 thus ———. Except for the curves showing notifications in 1955, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.







Infectious Diseases

A small decline occurred in the number of notifications of infectious diseases in England and Wales during the week ending March 26. The largest falls were 336 for measles, from 29,018 to 28,682, 57 for whooping-cough, from 1,924 to 1,867, and 24 for scarlet fever, from 839 to 815.

The largest declines in the incidence of measles were 422 in Lancashire, from 2,264 to 1,842, 348 in London, from 3,685 to 3,337, 239 in Derbyshire, from 1,053 to 814, 184 in Lincolnshire, from 1,361 to 1,177, 145 in Durham, from 986 to 841, 137 in Northumberland, from 972 to 835, and 125 in Kent, from 1,206 to 1,081, and the largest rises were 540 in Warwickshire, from 2,370 to 2,910, 163 in Middlesex, from 1,411 to 1,574, and 119 in Leicestershire, from 87 to 206. The only large fall in the returns of scarlet fever was 37 in Yorkshire West Riding, from 104 to 67. The chief fluctuations in the trends of whooping-cough were a rise of 41 in Cheshire, from 32 to 73, and a fall of 39 in Kent, from 134 to 95. 11 cases of diphtheria were notified, being 1 more than in the previous week.

10 cases of acute poliomyelitis were notified, and these were 4 fewer for paralytic and 1 more for non-paralytic cases than in the preceding week. The largest returns were Yorkshire West Riding 3 and London 2.

1,815 cases of dysentery were notified, being 1 less than the very high level recorded in the preceding week. The largest returns were Lancashire 629 (Oldham C.B. 157, Blackpool C.B. 155, Blackburn C.B. 58, Manchester C.B. 48, Liverpool C.B. 34, Chadderton U.D. 32, Whiston R.D. 18, Milnrow U.D. 16, Middleton M.B. 15, Preston R.D. 15, Southport C.B. 14, Crompton U.D. 10), London 204 (Hackney 91, Shoreditch 36, Islington 22, Southwark 10), Durham 177 (Sedgefield R.D. 35, South Shields C.B. 21, Seaham U.D. 20, Felling U.D. 19, Hebburn U.D. 18, Stanley U.D. 16, Easington R.D. 14), Northumberland 111 (Newcastle-upon-Tyne C.B. 27, Blyth M.B. 25, Bedlington U.D. 19, Hexham U.D. 10), Yorkshire West Riding 81 (Leeds C.B. 29, Dewsbury C.B. 18), Leicestershire 79 (Leicester C.B. 64), Norfolk 73 (Norwich C.B. 55), Lincolnshire 44 (Scunthorpe M.B. 29, Stamford M.B. 10), Warwickshire 43 (Birmingham C.B. 22, Nuneaton M.B. 16), Cheshire 38 (Stockport C.B. 26), Glamorganshire 35 (Cardiff C.B. 21), Northamptonshire 35 (Northampton C.B. 17), Surrey 33 (Carshalton U.D. 11), Yorkshire North Riding 25 (Middlesbrough C.B. 22), Rutland 22 (Oakham U.D. 22), Sussex 21 (Chichester R.D. 19), and Cumberland 20 (Whitehaven M.B. 12).

Scotland in 1954

The preliminary return for 1954 shows that the birth rate, 18.0 per 1,000 population, was slightly above the rates for the four preceding years. Infant mortality was 31 per 1,000 registered births and was the same as in 1953, which was the lowest recorded. The stillbirth rate, 25 per 1,000 total births, was also the same as in 1953. The death rate was 12.0 per 1,000 population, and was 0.5 above the rate for 1953 but 0.3 below the average of the five preceding years. The death rate from all forms of tuberculosis was 22 per 100,000 population and 20 from respiratory tuberculosis; these rates were 23 and 19, respectively, below the average of the five preceding years. The number of deaths from the principal epidemic diseases was 254, 133 fewer than in 1953. These deaths included 176 from influenza, 41 from meningococcal infections, 25 from whooping-cough, 8 from measles, 2 from diphtheria, 1 from typhoid, and 1 from scarlet fever. In addition there were 20 deaths from acute poliomyelitis.

Quarterly Returns for Scotland

The birth rate for the December quarter of 1954 was 17.0 per 1,000 population, being 0.1 below the rate for the December quarter of 1953 and 0.1 above the average of the five preceding fourth quarters. The infant mortality rate was 31 per 1,000 registered births; this was 1 below the rate for the corresponding quarter of 1953 and 8 below the five-years average. The general death rate was 11.9 per 1,000 population, being 0.6 more than in the December quarter of 1953 but 0.2 below the five-years average. The death rate from tuberculosis was 20 per 100,000 population and that for respiratory tuberculosis was 18; these rates were 22 and 19 respectively below the average of the five preceding fourth quarters. Deaths from the principal epidemic diseases numbered 78, including 62 from influenza, 10 from meningococcal infections, 5 from measles, and 1 from whooping-cough. No deaths were reported from diphtheria, scarlet fever, or typhoid.

Medical News

Ophthalmic Hospital of St. John.—Sir STEWART DUKE-ELDER has just returned from the tour of the Middle East which he undertook with the object of finding a site for the rebuilding of the Ophthalmic Hospital of St. John in Jerusalem (see *Journal*, March 12, p. 677). A new site for the hospital and the proposed research institute has been purchased outside the Old City, and it is hoped that the building will be finished by the end of 1956. The present hospital has 45 beds, but the new one will have 70 beds and, in addition, a special wing to house the research institute. The latter will have a separate staff, but will be under the overall control of the Order of St. John. The staff of the institute, when complete, will consist of a medical director, three British scientists, three Arab scientists, and a number of technicians. Research on trachoma will be an important part of the work of the institute. The initial cost of the hospital and institute is expected to be about £250,000.

Dr. Charles Hill.—It was announced from Downing Street on April 7 that Dr. CHARLES HILL, formerly Secretary of the British Medical Association, had succeeded Lord DE LA WARR as Postmaster-General. He had been Parliamentary Secretary at the Ministry of Food since 1951.

Poliomyelitis Vaccine.—Successful vaccination against poliomyelitis was claimed in the U.S.A. on April 12 for the vaccine developed by Dr. JONAS E. SALK. According to Press reports, Dr. T. FRANCIS stated that the vaccine was safe, effective, and potent. Preparations are now proceeding in the United States to make the vaccine widely available. In Britain, commenting on the news, a Medical Research Council spokesman said that two British pharmaceutical houses are already developing a similar vaccine. The firms concerned are understood to be Glaxo Laboratories and Burroughs Wellcome and Co.

Individual Efficiency in Industry.—A conference on "Individual Efficiency in Industry," arranged by a joint committee of the Medical Research Council and the Department for Scientific and Industrial Research, was held in Cambridge from March 31 to April 3, under the chairmanship of Sir GEOFFREY VICKERS, V.C. The conference was attended by both representatives of industry and research workers. The subjects discussed included the effects of environment and continuous work on performance, training problems, and the physiological and psychological aspects of machine design. The last session was on "The Industrial Application of Research Results." During the conference there were demonstrations at the Medical Research Council's unit for research on applied psychology and at the university engineering laboratories.

Hammersmith Premature Baby Unit.—A small party was held at the Hammersmith Hospital, London, on April 5 to welcome the 1,000th baby to be admitted to the premature baby unit. The unit was opened on December 1, 1947. Most of the babies cared for in the unit have been born in the obstetric department of the Hammersmith Hospital, but over one-third of admissions have been of babies born at home or in other hospitals and nursing-homes. About 800 nurses from Great Britain and 19 other countries have received periods of training from a few weeks to six months in the unit in the past seven years. In addition there have been over 7,000 visitors to the unit.

Birmingham University.—Mr. A. L. D'ABREU, part-time lecturer in surgery, has been given the title of reader in thoracic surgery. Dr. W. TREVOR COOKE has been appointed to a part-time readership in medicine.

Sir Harry Platt, P.R.C.S., is to receive the honorary LL.D. of Manchester University on May 11.

COMING EVENTS

Medical Art Society.—Annual exhibition at Walker's Galleries, 118, New Bond Street, London, W.1, from April 15 to 30, 10 a.m. to 5 p.m. (except Saturdays, 10 a.m. to 1 p.m.).

Institute of Diseases of the Chest.—Clinical demonstrations, open to medical practitioners without fee, will be given by Dr. J. G. SCADDING in the lecture-room of the Institute (in the grounds of the Brompton Hospital, Fulham Road, London, S.W.3) on Fridays at 5 p.m., from April 22 to July 8.

North-Western Tuberculosis Society.—A joint meeting with the British Tuberculosis Association is being held in the Clinical Sciences Building of Manchester University on April 22. The programme includes a symposium on chronic bronchitis. Details from Dr. M. J. GREENBERG, Manchester Chest Clinic, 352, Oxford Road, Manchester 13.

Medical Society for the Care of the Elderly.—Annual general meeting at the Whittington Hospital, London, N.19, on May 6 and 7. Details from the hon. secretary, Dr. A. N. EXTON-SMITH, at the Whittington Hospital.

NEW ISSUES

British Journal of Venereal Diseases.—The new issue (Vol. 31, No. 1) is now available. The contents include:

NORWAY CONQUERS VENEREAL DISEASES. Thomas D. Eliot.
TOPICAL CORTISONE IN SYPHILITIC INTERSTITIAL KERATITIS. Gordon O. Horne.
TREATMENT-RESISTANT SYPHILIS. R. V. Rajam and P. N. Rangiah.
YAWS IN MANCHESTER. Sydney M. Laird.
EFFECT OF ROOM TEMPERATURE ON SEROLOGIC TESTS FOR SYPHILIS. Hilfred N. Bossak, Ad Harris, and Sidney Olansky.
VDRL SLIDE FLOCCULATION REACTION FOR SYPHILIS PERFORMED ON ACTIVE SERA. Ekkehard E. Schmid and T. Velaudapillai.
COMPARISON OF THE IDE AND HARRIS (VDRL) SLIDE FLOCCULATION TESTS IN NIGERIA. L. R. Boulger and D. A. Cannon.

Thorax.—The new issue (Vol. 10, No. 1) is available. The contents include:

OSTEOPLASTIC THORACOPLASTY. Sir Russell Brock.
PATHOLOGICAL STUDIES OF MODIFIED PNEUMOCONIOSIS IN COAL-MINERS WITH RHEUMATOID ARTHRITIS (CAPLAN'S SYNDROME). J. Gough, D. Rivers, and R. M. E. Seal.
THE TECHNIQUE AND COMPLICATIONS OF PULMONARY VALVOTOMY WITH SPECIAL REFERENCE TO THE TRANSARTERIAL APPROACH. Frederik Therkelsen.
INDICATIONS FOR THORACIC AORTOGRAPHY. Walther Falholt, Gregers Thomsen, and H. Gosta Davidsen.
CLOSURE MECHANISMS AT THE CARDIA WITH SPECIAL REFERENCE TO THE DIAPHRAGMATICO-OESOPHAGEAL ELASTIC LIGAMENT. P. M. Peters.
DOUBLE AORTIC ARCH. R. E. Steen and S. J. Douglas.
RARE CARDIAC ANEURYSM IN A YOUNG ADULT. Kevin P. Clearkin and Henry Bunjé.
THE MANAGEMENT OF CONGENITAL OESOPHAGEAL ATRESIA AND TRACHEO-OESOPHAGEAL FISTULA. Keith D. Roberts, Ivo J. Carré, and James McN. Inglis.
SARCOMA OF THE OESOPHAGUS. D. Millar Bell.
NON-SPECIFIC OESOPHAGITIS. K. V. Lodge.
THE MECHANICS OF BREATHING IN NEWLY BORN BABIES. M. B. McIlroy and E. S. Tomlinson.
FRACTURE OF THE TRACHEA AND BRONCHUS. John Dark and P. Jewsbury.
AN ANALYTICAL REVIEW OF SPONTANEOUS HAEMOPNEUMOTHORAX. R. J. Calvert and Eric Smith.
TWO CASES OF INTRALOBAR SEQUESTRATION OF THE LUNG. C. McDowell, Douglas Robb, and J. S. Indyk.
MEDIASTINAL EMPHYSEMA AND ITS OCCURRENCE IN ARTIFICIAL PNEUMOPERITONEUM. C. S. Breathnach.

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SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Saturday, April 16

SOUTH-EAST METROPOLITAN REGIONAL TUBERCULOSIS SOCIETY.—At Bow Arrow Hospital, Dartford, 10.30 for 10.45 a.m., Dr. M. O. J. Gibson: Tuberculosis in Childhood.

Monday, April 18

INSTITUTE OF PSYCHIATRY.—5.30 p.m., lecture demonstration by Dr. E. Stengel.
MEDICAL SOCIETY OF LONDON.—8.30 p.m., First Lettsomian Lecture by Dr. J. G. Scadding: Treatment of Pulmonary Tuberculosis.
●ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5.15 p.m., Professor C. A. Wells: Cancer of the Bladder; 6.30 p.m., Mr. F. W. Holdsworth: Traumatic Paraplegia.

Tuesday, April 19

ILFORD MEDICAL SOCIETY.—At King George Hospital, Ilford, 8.45 p.m., Dr. Robert Forbes: Recent Developments in Medical Litigation.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Lumleian Lecture by Dr. A. M. Cooke: Some Aspects of Skeletal Disease.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor John Foster: Evaluation of Current Methods of Treatment of Idiopathic Stricture of the Valve of Krause.
SOCIETY FOR THE STUDY OF ADDICTION.—At Medical Society of London, 8 p.m., Mr. F. T. Hilliger: Handwriting in Relation to Drug Addiction and Alcoholism (illustrated).
SOUTH-WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, 8.30 p.m., Mr. K. M. Walker: Sexual Problems in General Practice.
WEST END HOSPITAL FOR NEUROLOGY AND NEUROSURGERY.—5.30 p.m., neurological demonstration by Dr. N. G. Hulbert.

Wednesday, April 20

CHADWICK TRUST.—At Reardon Smith Lecture Theatre, National Museum of Wales, Park Place, Cardiff, 3.30 p.m., Dr. N. R. Beattie: Role of the Public Health Inspector.
HYPNOTHERAPY GROUP.—At Royal Society of Medicine, 8 p.m., Dr. Denys E. R. Kelsey: Rationale of Hypno-Analysis.
MIDDLESEX COUNTY MEDICAL SOCIETY.—At London Airport, 2.30 p.m., tour; 5 p.m., Dr. A. S. R. Peffers: Transport of Sick Persons by Air.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Mr. A. W. Marsden, M.Sc.: Supply of Milk and Dairy Products to the Public (illustrated).

Thursday, April 21

GLASGOW UNIVERSITY MEDICO-CHIRURGICAL SOCIETY.—At Glasgow University Union, 7.30 p.m., debate with Dialectic Society.
ROYAL COLLEGE OF PHYSICIANS OF LONDON.—5 p.m., Lumleian Lecture by Dr. A. M. Cooke: Some Aspects of Skeletal Disease.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor N. R. Barrett: Primary Tumours of Rib.
●WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—7 p.m., dinner at Falstaff Hotel, 7.30 p.m., visit to Fleet Street; 9 p.m., lecture by Mr. W. Redpath: The Bones at St. Bride's; 10 p.m., to see the *Daily Express* "put to bed."

Friday, April 22

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., clinical demonstration by Dr. J. G. Scadding.

Any Questions ?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Serous Otitis

Q.—*A woman of 60 complains of intermittent deafness and gurgling noises in her ears for the last three years, worse in the morning. On auriscopic examination, bubbles are seen passing through clear fluid in the middle ear. This becomes more marked when the cheeks are blown out with the mouth and nose closed. What is the cause of this, and the treatment?*

A.—The appearance described by your correspondent suggests the presence of a clear fluid in the middle ear cavity, a condition known as serous otitis. Attention was drawn to the comparative frequency of this condition by Hoople and Blaisdell.[1] Since then it has been diagnosed more often, and it now appears to be one of the regular causes of conductive deafness. An allergic basis has been suggested for this condition, but the absence of eosinophils in the exudate or of other allergic manifestations makes this unlikely. It may be the result of blockage of the eustachian tube, and in fact some authorities feel that prolonged blockage of the eustachian tube is the most probable cause.

The treatment is removal of the fluid either by needle aspiration through the tympanic membrane or by making a small hole through the tympanic membrane with a paracentesis knife and blowing any fluid out by inflation through the eustachian tube. In some cases one such treatment is sufficient, but not infrequently repeated aspiration will be necessary. Efforts to clear the eustachian tube should not be overlooked. The possibility of mastoid drainage in persistent cases where there is a copious exudate may very occasionally have to be considered.

REFERENCE

[1] *Proc. roy. Soc. Med.*, **1944**, **37**, 270.

"Once a Caesarean"

Q.—*It not infrequently happens that a young healthy primipara with ample pelvic measurements has a caesarean section for a central placenta praevia. At a recent clinical meeting the statement was made that only one vaginal delivery should be allowed after this. What is your expert's opinion?*

A.—A similar statement is made by Professor Bruce T. Mayes, who, on page 424 of his *Practical Obstetrics* (Angus and Robertson; Sydney, 1954), writes: "If the patient has already had a vaginal delivery following caesarean I should do another caesarean," his argument being that the second pregnancy and labour may stretch and weaken the scar. Although this teaching may well be applied with profit to individual cases with special circumstances, it is not one which is widely accepted as a general principle. Indeed, if the uterine scar can be depended on to withstand only one labour, it could be argued with some force that it is illogical to allow the patient to risk vaginal delivery even of the second child, and that it is better to adopt the old rule of "Once a caesarean, always a caesarean," and to carry out three successive operations, sterilizing the patient at the third. The whole idea behind allowing the patient to attempt to deliver herself in the second pregnancy is that it will show whether her reproductive function is so unimpaired that she may continue to have a reasonably unrestricted number of further vaginal deliveries in the future if she wishes.

The management of a young woman who has previously had a caesarean section for a non-recurrent indication depends mainly on the details of the operation. If it is carried out through a *transverse* incision placed so low that it is wholly in the lower segment, and is done by an expert obstetrician working in good surroundings, the risk of the scar rupturing in any subsequent labour is very small. The exact extent of the risk is unknown, most of the published figures applying either to classical caesarean section or to a *vertical* incision in the lower segment, both of which are considerably more dangerous in this respect. Nevertheless, the transverse scar can rupture, and it may do so in one area only, and so silently that the accident is unrecognized. If this happens in the first labour after caesarean section, then in any subsequent labour, or indeed pregnancy, the defect may extend to involve the whole scar with serious results. Such an occurrence can be avoided by the following procedure.

Assuming the type and circumstances of the original section are favourable, the woman having her second baby should be allowed to deliver it vaginally provided the labour proceeds smoothly. As soon as the placenta is delivered, and before if the third stage is prolonged, the patient should be anaesthetized and a hand inserted into the uterus to examine the scar over its whole length. This is not only the best means of excluding a silent rupture in any part of it, but it allows an assessment of the thinness, width, and irregularity of the scar, which are fairly good guides to its strength from the standpoint of further childbearing. If the scar is found to be defective in any way the next baby should be delivered by caesarean section. If it is sound, and it usually is, there is no reason why future babies should not be delivered vaginally. One precaution which should always be taken, however, is that a woman who has a caesarean scar in the uterus should have *every* subsequent delivery in a fully equipped maternity hospital unit.

Estimation of Protein-bound Iodine

Q.—*Will you kindly give me references to the procedure for estimating protein-bound iodine, and describe the significance of the findings obtained?*

A.—Recent descriptions of the procedure will be found in the papers by de Mowbray and Tickner[1] and O'Neal and Simms.[2] The normal values run from 4 to 8 μg. per 100 ml. of plasma, and the test gives a good general correlation with alterations in thyroid function in both directions. However, high values may be seen without thyrotoxicosis in pregnancy and after previous iodine therapy. Values below normal without myxoedema have been reported in nephrosis. The technique is somewhat laborious and is not easily carried out in a busy routine laboratory.

REFERENCES

[1] *Lancet*, 1952, **2**, 511.
[2] *Amer. J. clin. Path.*, 1953, **23**, 493.

Side-effects of "Diamox"

Q.—*Two of my patients on the oral diuretic "diamox" developed peripheral neuritis within seven days. Each was having 250 mg. daily. The neuritis disappeared on discontinuing the drug. What are the side-effects of diamox, and is peripheral neuritis one? Is it safe to give diamox to these patients again, perhaps in a lower dosage?*

A.—Diamox (acetazoleamide) acts therapeutically by inhibiting the reabsorption of bicarbonate in the renal tubules, and so increasing the excretion of bicarbonate which carries with it base (sodium or potassium) into the urine. The most direct "side-effect" of diamox is thus to produce a lowering of the bicarbonate content of plasma—i.e., a metabolic acidosis. In patients on a low salt diet most of the base excreted may be potassium rather than sodium: the drug then fails in its object of reducing oedema, and

some potassium depletion may be induced. In high doses diamox can cause paraesthesiae, and also drowsiness and even psychosis; the mechanism of these neurological disturbances is not established. If the effect in the two patients mentioned is limited to tolerable subjective sensations, and the drug is otherwise effective, it should be continued; but more severe neurological involvement would be an indication for stopping the drug completely and trying other methods of therapeutic sodium depletion.

Acetylcholine in Psychiatry

Q.—*Acetylcholine has been used to treat cases of anxiety or obsessional behaviour. Could you give me further details about the type of case suitable for the treatment and the results obtained?*

A.—Acetylcholine treatment, as the inquirer states, has had its most successful effects in certain obsessional and anxiety states. The obsessional patients who have done best with it are those in whom the symptoms took predominantly the form of compulsive ruminations; patients in whom the ruminative tendency did not bulk large, but who suffered from repetitive routines of behaviour, etc., have not been found to respond nearly so well. Compulsive behaviour is usually little influenced by the treatment. The treatment is certainly worth trying in patients aged from 25 to 50—that is, neither the very young nor the old—and when the illness is not of very long duration. The tendency to rumination is reduced and the associated tension as a rule diminishes to a very satisfactory degree.

In patients suffering from anxiety states it is again the symptom of tension which is most favourably affected by the treatment. Fluctuating tension responds better than persistent tension. Anxiety states in which somatic symptoms, tachycardia, sweating, tremor, etc., are prominent do not do so well.

Persons of athletic build respond better than those of asthenic build. The treatment should not be given where there is any evidence of cardiac disease. Phillips and Hutchinson[1] in a selected series reported 70% improvements.

REFERENCE

[1] *British Medical Journal*, 1954, 1, 1468.

Trace Elements

Q.—*The agricultural community in which I work in Southern Rhodesia is very trace-element conscious, though most farmers lack the facilities and cash for accurate soil analysis. Undoubtedly our soils are poor, and one of the remedies suggested is the application of powdered seaweed. The argument is that dairy and poultry products from stock fed on crops grown with this as fertilizer will contain all the trace elements and be better human food. Is this correct?*

A.—The mineral nutrients essential for man are of two main groups; the first includes iron, calcium, sodium, potassium, phosphorus, and chloride, which are needed in considerably larger amounts than those in the second group, the trace elements proper, which are needed in exceedingly small quantities. The desirable dietary levels of some of these elements—e.g., copper, iodine, and fluorine—are known, but relatively little is known about those for such elements as cobalt, molybdenum, zinc, manganese, and magnesium, all of which are, however, known to be essential components of various biological systems.

It is generally believed that sufficient of each of the trace elements is present in ordinary diets; on the other hand, evidence of deficiency of such elements as cobalt and molybdenum has been recognized clinically in domestic animals. It would seem that the proper treatment of mineral deficiencies in livestock is to apply fertilizers containing the trace elements which are deficient in the soil so that the amounts of those elements in the crops are increased. Not only are adequately fertilized soils important for obtaining a satisfactory mineral content of the crops raised thereon, but the health and yields of crops and of livestock and the nutritional value of animal food products will be improved, and to the extent to which man obtains his food from such sources his dietary supply of the necessary trace elements will be secured.

The risk inherent in relying on a single source for a group of nutrients is that, in taking the amount necessary to supply some of them, certain other constituents may be taken in the wrong proportion. One example well known to South African farmers is the problem of administering to cattle minerals from certain sources: they are sometimes faced, when providing calcium and phosphorus, with the risk of producing fluorosis. Generally the procedure of choice is to inject the minerals which are in short supply into the biological cycle as a soil fertilizer, but, as in nutritional evaluations of food for man and animals, it is not enough merely to rely on chemical analyses. If indeed facilities for research are limited, it would be preferable to make suitable fertilizer trials rather than chemical analyses when trace-element deficiencies are suspected. As in animal nutrition, the new knowledge of "clinical" signs of malnutrition in plants, as well as yield data, may be used as criteria of the nutritional value of the soil and fertilizer. An outstanding exception to this general procedure is the correction of iodine deficiency by iodization of domestic salt.

Facial Hair in a Girl

Q.—*Have you any information, please, regarding the removal of facial hair in a girl of 18? Her mother asked me about electrolysis, but I think there is bound to be minute scarring after it, and I also understand that there is a general distribution of excess hairiness over the body. Menstruation is normal. I wondered whether there is any hormone treatment available.*

A.—In the great majority of cases no medical treatment is any good. In particular hormone treatment is valueless. However, a small minority of cases of hypertrichosis are due to adrenal hypertrophy, and this diagnosis should be excluded by urinary hormonal estimations.

Electrolysis, skilfully applied, leaves negligible scarring, but of course every hair has to be separately treated, and it is therefore not a very suitable method when the hypertrichosis is very severe or very widely distributed. It is worth noting that the popular view that shaving stimulates the growth of hair is untrue, and in many instances this is the best line of treatment if the patient can be persuaded to adopt it. It has to be admitted that our knowledge of this subject is at the present moment extremely small.

Corrections

In his article entitled "A Purpuric Drug Eruption Caused by Carbromal" (March 12, p. 645), Dr. Peter Borrie mentioned that preparations containing carbromal are being fairly widely advertised to the public. In this connexion CLINICAL PRODUCTS LTD. write: "We wish to avoid any misunderstanding by pointing out that 'persomnia' public advertising was discontinued in June, 1950, and 'dormiprin' has never been advertised to the public."

In the last sentence of the first paragraph of Dr. H. S. Russell's letter (*Journal*, April 9, p. 909) on "Post-maturity and Asphyxia," "intact peritoneum" should have read "intact perineum."

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 4499. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

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